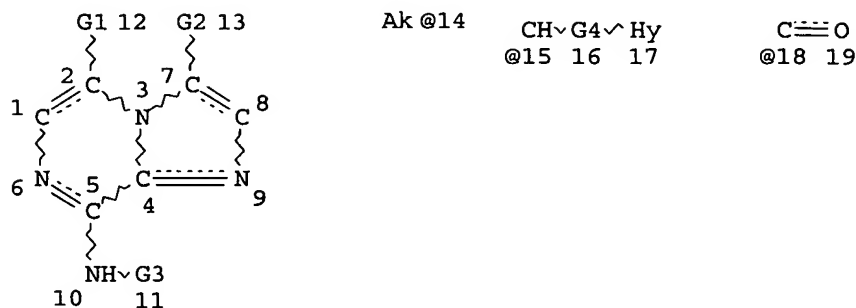


=> d stat que l29; d his nofile
L21 STR



VAR G1=H/X/14
VAR G2=H/X/CY/14/CF3
VAR G3=CB/15/SO2/18
REP G4=(0-3) CH
NODE ATTRIBUTES:
CONNECT IS E1 C AT 1
CONNECT IS E1 RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L29 474 SEA FILE=REGISTRY SSS FUL L21

100.0% PROCESSED 10269 ITERATIONS
SEARCH TIME: 00.00.01

474 ANSWERS

(FILE 'HOME' ENTERED AT 11:42:44 ON 19 JUN 2006)

FILE 'CAPLUS' ENTERED AT 11:43:03 ON 19 JUN 2006

SET LINE 250
SET DETAIL OFF
E US2003-666424/AP, PRN 25
SET NOTICE 1000 SEARCH
L1 1 SEA ABB=ON US2003-666424/AP
SET NOTICE LOGIN SEARCH
SET LINE LOGIN
SET DETAIL LOGIN
L2 33 SEA ABB=ON PARUCH K?/AU
L3 48 SEA ABB=ON GUZI T?/AU
L4 127 SEA ABB=ON DWYER M?/AU
L5 236 SEA ABB=ON DOLL R?/AU
L6 266 SEA ABB=ON GIRIJAVALLABHAN V?/AU
L7 14 SEA ABB=ON L2 AND L3 AND L4 AND L5 AND L6

FILE 'STNGUIDE' ENTERED AT 11:44:30 ON 19 JUN 2006

FILE 'MEDLINE, DRUGU, WPIX, BIOSIS, EMBASE' ENTERED AT 11:46:29 ON 19 JUN

2006

L8 29 SEA ABB=ON PARUCH K?/AU
L9 65 SEA ABB=ON GUZI T?/AU
L10 366 SEA ABB=ON DWYER M?/AU
L11 1429 SEA ABB=ON DOLL R?/AU
L12 468 SEA ABB=ON GIRIJAVALLABHAN V?/AU
L13 869202 SEA ABB=ON KINASE#
L14 38816 SEA ABB=ON ?PYRAZIN?
L15 11 SEA ABB=ON L8 AND L9 AND L10 AND L11 AND L12
L16 48 SEA ABB=ON (L8 OR L9 OR L10 OR L11 OR L12) AND (L13 OR L14)
L17 8 SEA ABB=ON (L8 OR L9 OR L10 OR L11 OR L12) AND L13 AND L14

FILE 'MEDLINE, DRUGU, WPIX, BIOSIS, EMBASE' ENTERED AT 11:48:19 ON 19 JUN 2006

D QUE L15
D QUE L17
L18 16 SEA ABB=ON L15 OR L17

FILE 'CAPLUS' ENTERED AT 11:48:36 ON 19 JUN 2006

D QUE L1
D QUE L7
L19 14 SEA ABB=ON L1 OR L7

FILE 'CAPLUS, WPIX' ENTERED AT 11:48:46 ON 19 JUN 2006

L20 18 DUP REM L19 L18 (12 DUPLICATES REMOVED)
ANSWERS '1-10' FROM FILE CAPLUS
ANSWERS '11-18' FROM FILE WPIX
D IBIB ED ABS HITIND 1-10
D IALL ABEQ TECH 11-18

FILE 'STNGUIDE' ENTERED AT 11:49:31 ON 19 JUN 2006

FILE 'REGISTRY' ENTERED AT 11:52:06 ON 19 JUN 2006

L21 STR
L22 29 SEA SSS SAM L21

FILE 'CAPLUS' ENTERED AT 11:56:40 ON 19 JUN 2006

L23 10 SEA ABB=ON L22
SEL RN L1

FILE 'REGISTRY' ENTERED AT 11:57:01 ON 19 JUN 2006

L24 112 SEA ABB=ON (100286-90-6/BI OR 10540-29-1/BI OR 11056-06-7/BI
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57-63-6/BI OR 58-05-9/BI OR 58-18-4/BI OR 58-22-0/BI OR

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OR 9015-68-3/BI OR 95058-81-4/BI OR 968-93-4/BI OR 97682-44-5/B
I)
D SCAN

FILE 'STNGUIDE' ENTERED AT 11:57:53 ON 19 JUN 2006

FILE 'REGISTRY' ENTERED AT 12:00:44 ON 19 JUN 2006

L25 STR L21
L26 9 SEA SSS SAM L21 NOT L25

FILE 'CAPLUS' ENTERED AT 12:03:19 ON 19 JUN 2006

L27 5 SEA ABB=ON L26

FILE 'REGISTRY' ENTERED AT 12:03:35 ON 19 JUN 2006

L28 29 SEA SSS SAM L21
L29 474 SEA SSS FUL L21
SAVE TEMP L29 WAR424FULL/A
E C16H18BRN5/MF
L30 200 SEA ABB=ON C16H18BRN5?/MF
L31 2 SEA ABB=ON L30 AND L29
D SCAN
L32 2 SEA ABB=ON L31 AND IMIDAZO
L33 1 SEA ABB=ON L31 AND 3-BROMO

FILE 'REGISTRY' ENTERED AT 12:05:25 ON 19 JUN 2006

D STAT QUE L31
D STAT QUE L29
D QUE NOS L33
D IDE L33

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 12:06:33 ON 19 JUN 2006

L34 3 SEA ABB=ON L33
L35 2 DUP REM L34 (1 DUPLICATE REMOVED)
ANSWER '1' FROM FILE CAPLUS
ANSWER '2' FROM FILE USPATFULL
D IBIB ED ABS HITRN 1-2

FILE 'CAPLUS' ENTERED AT 12:07:07 ON 19 JUN 2006

L36 16 SEA ABB=ON L29

FILE 'REGISTRY' ENTERED AT 12:07:25 ON 19 JUN 2006

L37 ANALYZE L29 1- LC : 5 TERMS
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FILE 'REGISTRY' ENTERED AT 12:08:24 ON 19 JUN 2006

D STAT QUE L29

FILE 'CAPLUS' ENTERED AT 12:08:24 ON 19 JUN 2006

D QUE NOS L36
L38 15 SEA ABB=ON L36 NOT L33

D IBIB ED ABS HITSTR L38 1-15

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D STAT QUE L29

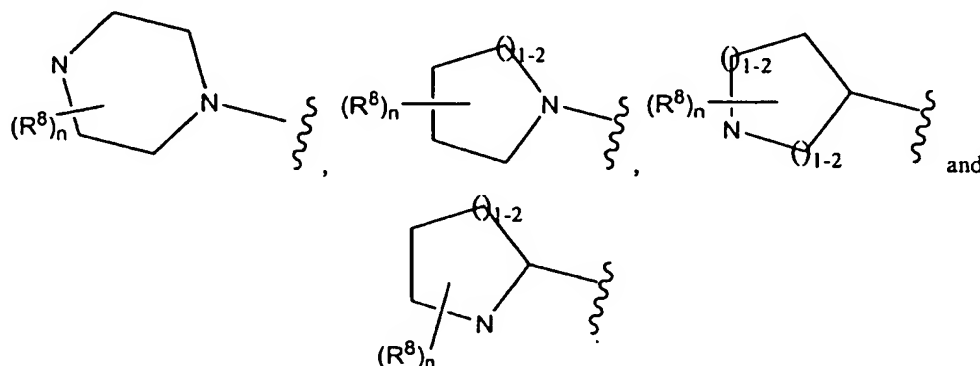
=>

treatment of neurodegenerative diseases such Alzheimer's disease, cardiovascular diseases, viral diseases and fungal diseases.

Detailed Description

5 In one embodiment, the present invention discloses imidazo[1,2-a]pyrazine compounds which are represented by structural Formula III, or a pharmaceutically acceptable salt or solvate thereof, wherein the various moieties are as described above.

10 In a preferred embodiment, R is selected from the group consisting of alkyl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, arylalkyl,



wherein each of said alkyl, heteroaryl, cycloalkyl, arylalkyl, heterocyclyl and the heterocyclyl moieties shown above for R can be unsubstituted or optionally
 15 independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, cycloalkyl, CF_3 , CN, $-\text{OCF}_3$, $-\text{OR}^6$, $-\text{C}(\text{O})\text{R}^7$, $-\text{NR}^5\text{R}^6$, $-\text{C}(\text{O}_2)\text{R}^6$, $-\text{C}(\text{O})\text{NR}^5\text{R}^6$, $-\text{SR}^6$, $-\text{S}(\text{O}_2)\text{R}^7$, $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$, $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$, $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ and $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^6$.

20 In another preferred embodiment, R^1 is H or halogen.

In another preferred embodiment, R^2 is selected from the group consisting of H, halogen, cycloalkyl, CN, alkynyl and $-\text{CF}_3$.

In another preferred embodiment, R^3 is selected from the group consisting of aryl, heteroaryl, heterocyclyl, $-(\text{CHR}^5)_n$ -heteroaryl, $-\text{S}(\text{O}_2)\text{R}^6$, $-\text{C}(\text{O})\text{R}^6$,

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=> fil medl drugu wpix biosis embase; d que l15; d que l17; s l15 or l17
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FILE 'DRUGU' ENTERED AT 11:48:19 ON 19 JUN 2006
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L8 29 SEA PARUCH K?/AU
L9 65 SEA GUZI T?/AU
L10 366 SEA DWYER M?/AU
L11 1429 SEA DOLL R?/AU
L12 468 SEA GIRIJAVALLABHAN V?/AU
L15 11 SEA L8 AND L9 AND L10 AND L11 AND L12

*inventor
search*

L8 29 SEA PARUCH K?/AU
L9 65 SEA GUZI T?/AU
L10 366 SEA DWYER M?/AU
L11 1429 SEA DOLL R?/AU
L12 468 SEA GIRIJAVALLABHAN V?/AU
L13 869202 SEA KINASE#
L14 38816 SEA ?PYRAZIN?
L17 8 SEA (L8 OR L9 OR L10 OR L11 OR L12) AND L13 AND L14

L18 16 L15 OR L17

=> fil capl; d que l1; d que l7
FILE 'CAPLUS' ENTERED AT 11:48:36 ON 19 JUN 2006
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FILE COVERS 1907 - 19 Jun 2006 VOL 144 ISS 26
FILE LAST UPDATED: 18 Jun 2006 (20060618/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L1 1 SEA FILE=CAPLUS ABB=ON US2003-666424/AP

L2 33 SEA FILE=CAPLUS ABB=ON PARUCH K?/AU
 L3 48 SEA FILE=CAPLUS ABB=ON GUZI T?/AU
 L4 127 SEA FILE=CAPLUS ABB=ON DWYER M?/AU
 L5 236 SEA FILE=CAPLUS ABB=ON DOLL R?/AU
 L6 266 SEA FILE=CAPLUS ABB=ON GIRIJAVALLABHAN V?/AU
 L7 14 SEA FILE=CAPLUS ABB=ON L2 AND L3 AND L4 AND L5 AND L6

=> s l1 or l7

L19 14 L1 OR L7

=> dup rem l19,l18

FILE 'CAPLUS' ENTERED AT 11:48:46 ON 19 JUN 2006
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PROCESSING COMPLETED FOR L19

PROCESSING COMPLETED FOR L18

L20 18 DUP REM L19 L18 (12 DUPLICATES REMOVED)
 ANSWERS '1-10' FROM FILE CAPLUS
 ANSWERS '11-18' FROM FILE WPIX

=> d ibib ed abs hitind 1-10; d iall abeq tech 11-18

L20 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2004:267335 CAPLUS

DOCUMENT NUMBER: 140:287379

TITLE: Preparation and pharmaceutical compositions of novel
 pyrazolopyridines as cyclin dependent kinase
 inhibitors

INVENTOR(S): Dwyer, Michael P.; Guzi, Timothy J.
 ; Paruch, Kamil; Doll, Ronald J.;
 Keertikar, Kartik M.; Girijavallabhan, Viyyoor
 M.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026872	A1	20040401	WO 2003-US29841	20030917
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD,				

MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE,
SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2499593 AA 20040401 CA 2003-2499593 20030917
AU 2003270846 A1 20040408 AU 2003-270846 20030917
US 2004097516 A1 20040520 US 2003-664337 20030917
EP 1539750 A1 20050615 EP 2003-752559 20030917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
CN 1681816 A 20051012 CN 2003-822011 20030917
JP 2006503060 T2 20060126 JP 2004-538405 20030917
ZA 2005002271 A 20050919 ZA 2005-2271 20050317
PRIORITY APPLN. INFO.: US 2002-412138P P 20020919
WO 2003-US29841 W 20030917
OTHER SOURCE(S): MARPAT 140:287379
ED Entered STN: 01 Apr 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB In its many embodiments, the present invention provides a novel class of pyrazolo[1,5-*a*pyridine compds. I [R = (un)substituted-alkyl, -aryl, -heteroaryl, -heteroarylalkyl, etc.; R1 = H, alkyl or aryl; R2 = H, (un)substituted-alkyl, -alkenyl, -alkynyl, -aryl, etc.; R3 = H, halo, CF3, (un)substituted-alkyl, -aryl, etc.; R4 = H, halo, CF3, (un)substituted-alkyl, -cycloalkyl, -aryl, -heteroaryl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by condensation of 7-amino-5-phenylpyrazolo[1,5-*a*pyridine (preparation given) with 3-formylpyridine. I possessed excellent CDK inhibitory properties as demonstrated by the IC50 value for III of 0.078 μ M in inhibition of CDK2.

IC ICM C07D471-04

ICS A61K031-437; A61P035-00

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:267330 CAPLUS

DOCUMENT NUMBER: 140:303698

TITLE: Preparation and pharmaceutical compositions of novel imidazopyridines as cyclin dependent kinase inhibitors

INVENTOR(S): Dwyer, Michael P.; Guzi, Timothy J.
; Paruch, Kamil; Doll, Ronald J.;
Keertikar, Kartik M.; Girijavallabhan, Viyyoor
M.

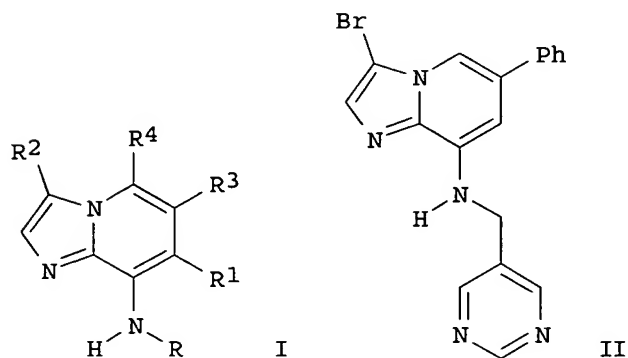
PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026867	A2	20040401	WO 2003-US29498	20030917
WO 2004026867	A3	20040805		
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CA 2499639	AA	20040401	CA 2003-2499639	20030917
AU 2003295332	A1	20040408	AU 2003-295332	20030917
US 2004097517	A1	20040520	US 2003-664338	20030917
US 6992080	B2	20060131		
EP 1539756	A2	20050615	EP 2003-786514	20030917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006507254	T2	20060302	JP 2004-538237	20030917
US 2006030555	A1	20060209	US 2005-238597	20050929
PRIORITY APPLN. INFO.:			US 2002-412063P	P 20020919
			US 2003-664338	A3 20030917
			WO 2003-US29498	W 20030917

OTHER SOURCE(S): MARPAT 140:303698
 ED Entered STN: 01 Apr 2004
 GI



AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyridine compds. I [R = (un)substituted-alkyl, -aryl, -heteroaryl, -heterocyclyl, etc.; R¹ = H, alkyl or aryl; R² = H, (un)substituted-alkyl, -aryl, arylalkyl, alkenyl, etc.; R³ = H, halo, CF₃, (un)substituted-alkyl, -aryl, etc.; R⁴ = H, halo, CF₃,

(un)substituted-alkyl, -cycloalkyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was made by condensation of 8-amino-3-bromo-6-phenylimidazopyridine (preparation given) with 5-formylpyrimidine. In inhibition assays with CDK2, I possessed excellent inhibitory properties, e.g., II possessed an IC50 value of 0.12 μ M.

IC ICM C07D471-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

L20 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:267246 CAPLUS

DOCUMENT NUMBER: 140:303696

TITLE: Preparation and pharmaceutical compositions of novel imidazopyrazines as cyclin dependent kinase inhibitors

INVENTOR(S): Paruch, Kamil; Guzi, Timothy J.;
Dwyer, Michael P.; Doll, Ronald J.;
Girijavallabhan, Viyyoor M.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

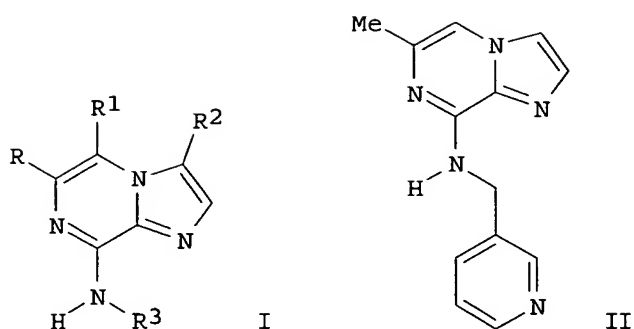
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026310	A1	20040401	WO 2003-US29456	20030919
WO 2004026310	C1	20050630		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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AU 2003275031	A1	20040408	AU 2003-275031	20030919
US 2004072835	A1	20040415	US 2003-666424	20030919 <--
EP 1542693	A1	20050622	EP 2003-759300	20030919
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006503838	T2	20060202	JP 2004-538213	20030919
ZA 2005002380	A	20050927	ZA 2005-2380	20050322
PRIORITY APPLN. INFO.:			US 2002-412906P	P 20020923
			WO 2003-US29456	W 20030919

OTHER SOURCE(S): MARPAT 140:303696

ED Entered STN: 01 Apr 2004

GI



AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compds. I [R = CF₃, (un)substituted-alkyl, -heteroaryl, -heteroarylalkyl, -cycloalkyl, -heterocyclyl, etc.; R₁ = H, halo or alkyl; R₂ = H, halo, CN, cycloalkyl, heterocyclyl, alkynyl and CF₃; R₃ = aryl (with exception of Ph), (un)substituted-heteroaryl (with exception of furyl), -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by substitution of 8-chloro-6-methylimidzol[1,2-a]pyrazine with 3-(aminomethyl)pyridine. Methods for performing assays with I are described (no data).

IC ICM A61K031-5025

ICS A61K031-407; A61K031-4406; A61K031-4427; C07D487-04

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2004:269996 CAPLUS

DOCUMENT NUMBER: 140:303691

TITLE: Preparation and pharmaceutical compositions of novel pyrazolopyrimidines as cyclin dependent kinase inhibitors

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Doll, Ronald J.; Girijavallabhan, Viyyoor Moopil; Alvarez, Carmen S.; Chan, Tin-Yau; Knutson, Chad; Madison, Vincent; Fischmann, Thierry O.; Dillard, Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray Anthony; Park, Haengsoon

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia, Inc.

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

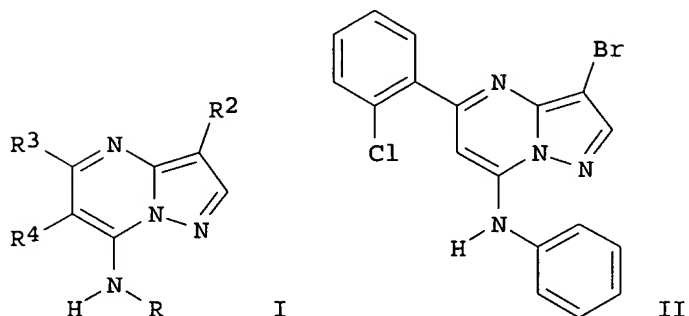
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004026229 A2 20040401 WO 2003-US27491 20030903
 WO 2004026229 A3 20040617
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,
 ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD,
 MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE,
 SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2497544 AA 20040401 CA 2003-2497544 20030903
 AU 2003298571 A1 20040408 AU 2003-298571 20030903
 EP 1534712 A2 20050601 EP 2003-796321 20030903
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 JP 2006502184 T2 20060119 JP 2004-537708 20030903
 ZA 2005001846 A 20050912 ZA 2005-1846 20050303
 PRIORITY APPLN. INFO.: US 2002-408029P P 20020904
 WO 2003-US27491 W 20030903
 OTHER SOURCE(S): MARPAT 140:303691
 ED Entered STN: 02 Apr 2004
 GI



AB In its many embodiments, the present invention provides a novel class of pyrazolo[1,5-a]pyrimidine compds. I [R = (un)substituted aryl; R² = halo, CN, (un)substituted alkyl, etc.; R³ = H, halo, (un)substituted-alkyl, -alkynyl, -aryl, etc.; R⁴ = H, halo or alkyl] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by substitution of 3-bromo-7-chloro-5-(2-chlorophenyl)-pyrazolo[1,5-a]pyrimidine (preparation given) with aniline. I exhibit excellent CDK inhibitory properties as demonstrated by II which possessed a IC₅₀ value of 0.51 μ M in kinase activity assays.

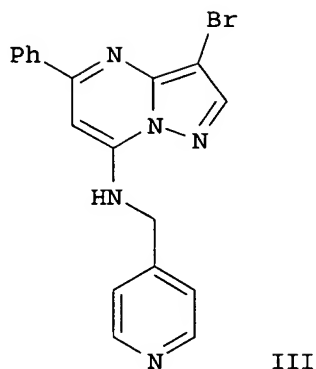
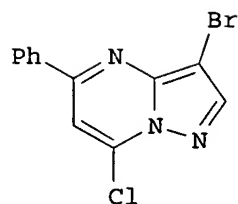
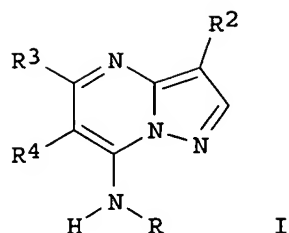
IC ICM A61K

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63

L20 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
 ACCESSION NUMBER: 2004:265849 CAPLUS

DOCUMENT NUMBER: 140:321371
 TITLE: Preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors
 INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil;
 Dwyer, Michael P.; Doll, Ronald J.;
 Girijavallabhan, Viyyoor Moopil; Mallams, Alan; Alvarez, Carmen S.; Keertikar, Kartik M.; Rivera, Jocelyn; Chan, Tin-yau; Madison, Vincent; Fischmann, Thierry O.; Dillard, Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray Anthony; Park, Haengsoon; Paradkar, Vidyadhar M.; Hobbs, Douglas Walsh
 PATENT ASSIGNEE(S): Schering Corporation, USA
 SOURCE: PCT Int. Appl., 609 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022561	A1	20040318	WO 2003-XB27555	20030903
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CN 1735614	A	20060215	CN 2003-824997	20030903
PRIORITY APPLN. INFO.:			US 2002-408027P	P 20020904
			US 2002-421959P	P 20021029
ED	Entered STN:	01 Apr 2004		
GI				



AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020 μ M and 0.029 μ M against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a

Part

III of I-III series.

IC ICM C07D487-04

ICS A61K031-519; C07D239-00; C07D231-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

L20 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2004:220335 CAPLUS

DOCUMENT NUMBER: 140:270872

TITLE: Preparation of pyrazolo[1,5-a]pyrimidines as cyclin dependent kinase inhibitors and anticancer agents

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil;
Dwyer, Michael P.; Doll, Ronald J.;
Girijavallabhan, Viyyoor Moopil; Dillard,
Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray
Anthony; Park, Haengsoon

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia, Inc.;
Pharmacopeia Drug Discovery, Inc.

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

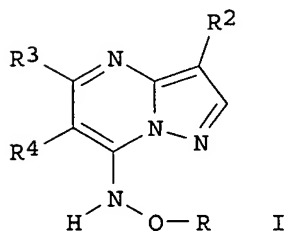
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022560	A1	20040318	WO 2003-US27502	20030903
WO 2004022560	C2	20050707		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2497450	AA	20040318	CA 2003-2497450	20030903
AU 2003268385	A1	20040329	AU 2003-268385	20030903
US 2004116442	A1	20040617	US 2003-653868	20030903
EP 1534710	A1	20050601	EP 2003-749347	20030903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006502161	T2	20060119	JP 2004-534459	20030903
ZA 2005001852	A	20050908	ZA 2005-1852	20050303
PRIORITY APPLN. INFO.:			US 2002-407999P	P 20020904
			WO 2003-US27502	W 20030903
OTHER SOURCE(S): MARPAT 140:270872				
ED Entered STN: 19 Mar 2004				
GI				



AB The title compds. [I; Q = SO₂, CO; R = each (un)substituted aryl or heteroaryl; R₂ = cyano, NR₅R₆, CO₂R₆, CONR₅R₆, OR₆, SR₆, SO₂R₇, SO₂NR₅R₆, -N(R₅)SO₂R₇, N(R₅)COR₇, N(R₅)CONR₅R₆, alkynyl, heteroaryl, CF₃, heterocyclyl, alkynylalkyl, cycloalkyl, (un)substituted alkyl; R₃ = H, halogen, NR₅R₆, CONR₅R₆, each (un)substituted alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, etc.; R₄ = H, halo, alkyl; R₅ = H, alkyl; R₆ = H, each (un)substituted alkyl, aryl, arylalkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; or R₅ and R₆ in the moiety -NR₅R₆, may be joined together to form an (un)substituted cycloalkyl or heterocyclyl] or pharmaceutically acceptable salts or solvates thereof are prepared. In its many embodiments, the present invention also provides methods of preparing such compds., pharmaceutical compns. containing one or more such compds. I, methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or

more diseases associated with cyclin dependent kinase using such compds. I or pharmaceutical compns. The disease associated with cyclin dependent kinase is selected from the group consisting of; (1) cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous cell carcinoma; (2) leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, hairy cell lymphoma and Burkitt's lymphoma; (3) acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia; (4) fibrosarcoma and rhabdomyosarcoma; (5) astrocytoma, neuroblastoma, glioma and schwannomas; and (6) melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoacanthoma, thyroid follicular cancer and Kaposi's sarcoma.

IC ICM C07D487-04

ICS A61K031-519; A61P025-00; A61P035-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 7

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2004:220334 CAPLUS

DOCUMENT NUMBER: 140:270871

TITLE: Preparation of pyrazolo[1,5-a]pyrimidines as cyclin dependent kinase inhibitors and anticancer agents

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil;
Dwyer, Michael P.; Doll, Ronald J.;
Girijavallabhan, Viyyoor Moopil; Dillard,
Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray
Anthony; Park, Haengsoon

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia, Inc.

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022559	A1	20040318	WO 2003-US27405	20030903
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2497444	AA	20040318	CA 2003-2497444	20030903
AU 2003268357	A1	20040329	AU 2003-268357	20030903
EP 1534709	A1	20050601	EP 2003-749317	20030903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006501260	T2	20060112	JP 2004-534424	20030903
CN 1738821	A	20060222	CN 2003-824448	20030903
ZA 2005001851	A	20050908	ZA 2005-1851	20050303
PRIORITY APPLN. INFO.:			US 2002-408030P	P 20020904

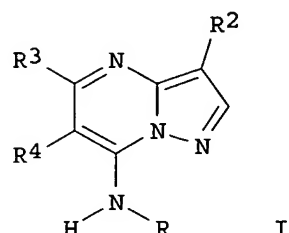
WO 2003-US27405

W 20030903

OTHER SOURCE(S): MARPAT 140:270871

ED Entered STN: 19 Mar 2004

GI



AB The title compds. [I; R = (un)substituted heteroaryl; R2 = (un)substituted alkyl, alkynyl, aryl, heteroaryl, alkynylalkyl, CF3, heterocyclalkyl, alkynylalkyl, cycloalkyl, CO2R4, etc., wherein aryl is optionally substituted; R3 = H, halogen, NR5R6, CO2R4, CONR5R6, each (un)substituted alkyl, alkynyl, cycloalkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocycl, heterocyclalkyl, or heteroaryl, etc.; R4 = H, halo, alkyl; R5 = H, alkyl; R6 = H, each (un)substituted alkyl, aryl, arylalkyl, cycloalkyl, heterocycl, heterocyclalkyl, heteroaryl, or heteroarylalkyl; or R5 and R6 in the moiety -NR5R6, may be joined together to form an (un)substituted cycloalkyl or heterocycl] or pharmaceutically acceptable salts or solvates thereof are prepared. In its many embodiments, the present invention also provides methods of preparing such compds., pharmaceutical compns. containing one or more such compds. I, methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with cyclin dependent kinase using such compds. I or pharmaceutical compns. The disease associated with cyclin dependent kinase is selected from the group consisting of; (1) cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous cell carcinoma; (2) leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, hairy cell lymphoma and Burkitt's lymphoma; (3) acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia; (4) fibrosarcoma and rhabdomyosarcoma; (5) astrocytoma, neuroblastoma, glioma and schwannomas; and (6) melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoacanthoma, thyroid follicular cancer and Kaposi's sarcoma.

IC ICM C07D487-04

ICS A61K031-519; A61P025-00; A61P035-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 7

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

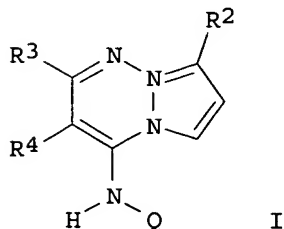
ACCESSION NUMBER: 2004:220207 CAPLUS

DOCUMENT NUMBER: 140:270868

TITLE: Preparation of pyrazolo[1,5-a]pyrimidines as cyclin dependent kinase inhibitors and anticancer agents

INVENTOR(S) : Guzi, Timothy J.; Paruch, Kamil;
 Dwyer, Michael P.; Doll, Ronald J.;
 Girijavallabhan, Viyyoor Moopil; Knutson,
 Chad; Mckittrick, Brian; Dillard, Lawrence W.; Tran,
 Vinh D.; He, Zhen Min; James, Ray Anthony; Park,
 Haengsoon
 PATENT ASSIGNEE(S) : Schering Corporation, USA; Pharmacopeia, Inc.
 SOURCE: PCT Int. Appl., 77 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022062	A1	20040318	WO 2003-US27564	20030903
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2497539	AA	20040318	CA 2003-2497539	20030903
AU 2003265901	A1	20040329	AU 2003-265901	20030903
US 2004102452	A1	20040527	US 2003-654163	20030903
EP 1545533	A1	20050629	EP 2003-794594	20030903
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JP 2006500391	T2	20060105	JP 2004-534490	20030903
ZA 2005001854	A	20050912	ZA 2005-1854	20050303
PRIORITY APPLN. INFO.:			US 2002-408182P	P 20020904
			WO 2003-US27564	W 20030903
OTHER SOURCE(S) : MARPAT 140:270868				
ED Entered STN: 19 Mar 2004				
GI				



AB The title compds. [I; Q = SO₂NR₆R₇, CONR₆R₇, CO₂R₇; R₂ = (un)substituted alkyl, alkynyl, alkynylalkyl, cycloalkyl, CF₃, CO₂R₆, aryl, arylalkyl, heteroarylalkyl, heterocyclyl, etc., wherein aryl is optionally substituted; R₃ = H, halogen, NR₅R₆, CONR₅R₆, CO₂R₄, each (un)substituted alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, etc.; R₄ = H, halo,

alkyl; R5 = H, alkyl; R6 = H, each (un)substituted alkyl, aryl, arylalkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; R7 = each (un)substituted alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl; or R5 and R6 in the moiety -NR5R6, may be joined together to form an (un)substituted cycloalkyl or heterocyclyl or pharmaceutically acceptable salts or solvates thereof are prepared. In its many embodiments, the present invention also provides methods of preparing such compds., pharmaceutical compns. containing one or

more

such compds. I, methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with cyclin dependent kinase using such compds. I or pharmaceutical compns. The disease associated with cyclin dependent kinase is selected from the group consisting of; (1) cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous cell carcinoma; (2) leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, hairy cell lymphoma and Burkitt's lymphoma; (3) acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia; (4) fibrosarcoma and rhabdomyosarcoma; (5) astrocytoma, neuroblastoma, glioma and schwannomas; and (6) melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoacanthoma, thyroid follicular cancer and Kaposi's sarcoma.

IC ICM A61K031-50

ICS A61P035-00; C07D487-04; C07D239-00; C07D231-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 7

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2004:981365 CAPLUS

DOCUMENT NUMBER: 141:379943

TITLE: Preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil;
Dwyer, Michael P.; Doll, Ronald J.;
Girijavallabhan, Viyyoor M.; Mallams, Alan;
Alvarez, Carmen S.; Keertikar, Kartik M.; Rivera, Jocelyn; Chan, Tin-Yau; Madison, Vincent; Fischmann, Thierry O.; Dillard, Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray Anthony; Park, Haengsoon;
Paradkar, Vidyadhar M.; Hobbs, Douglas Walsh

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacoopia, Inc.

SOURCE: U.S. Pat. Appl. Publ., 1044 pp., Cont.-in-part of U.S. Ser. No. 654,546.

CODEN: USXXCO

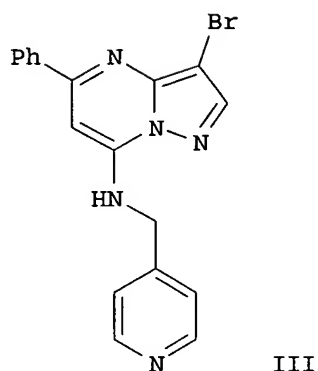
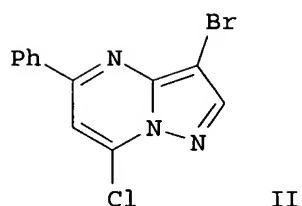
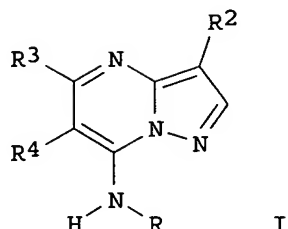
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004209878	A1	20041021	US 2004-776988	20040211
US 2004209878	A1	20041021	US 2004-776988	20040211
PRIORITY APPLN. INFO.:			US 2002-408027P	P 20020904
			US 2002-421959P	P 20021029

US 2003-654546
US 2004-776988A2 20030903
A 20040211ED Entered STN: 17 Nov 2004
GI

AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared. Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020 μ M and 0.029 μ M against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a

Part

III of I-III series.

IC ICM A61K031-5377

ICS A61K031-519; C07D487-04

INCL 514234500; 514252160; 514259300; 544117000; 544280000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

L20 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:267339 CAPLUS

DOCUMENT NUMBER: 140:303700

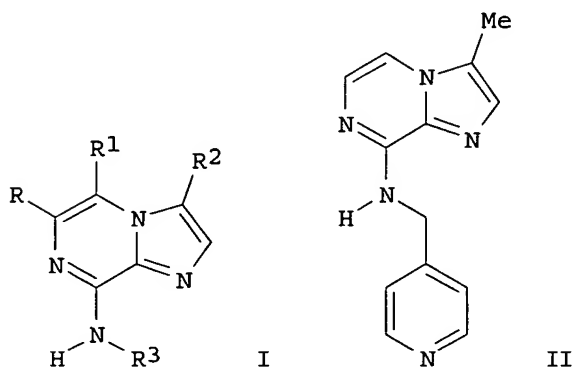
TITLE: Preparation and pharmaceutical compositions of novel imidazopyrazines as cyclin dependent kinase inhibitors

INVENTOR(S): Paruch, Kamil; Guzi, Timothy J.;
Dwyer, Michael P.; Doll, Ronald J.;
Girijavallabhan, Viyyoor M.; Mallams, Alan K.

PATENT ASSIGNEE(S): Schering Corporation, USA
 SOURCE: PCT Int. Appl., 82 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026877	A1	20040401	WO 2003-US29209	20030919
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2499756	AA	20040401	CA 2003-2499756	20030919
AU 2003272476	A1	20040408	AU 2003-272476	20030919
EP 1543008	A1	20050622	EP 2003-754658	20030919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1694886	A	20051109	CN 2003-825177	20030919
JP 2006507253	T2	20060302	JP 2004-537904	20030919
ZA 2005002375	A	20050927	ZA 2005-2375	20050322
PRIORITY APPLN. INFO.:			US 2002-412997P	P 20020923
			WO 2003-US29209	W 20030919

OTHER SOURCE(S): MARPAT 140:303700
 ED Entered STN: 01 Apr 2004
 GI



AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compds. of formula I [R = H, halo, (un)substituted-aryl, -heteroaryl, -cycloalkyl, etc.; R1 = H, halo or alkyl; R2 = halo, (un)substituted-alkyl, -aryl, -arylalkyl, etc.; R3 = H, (un)substituted-aryl, -heteroaryl, -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical

formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by condensation of 8-chloro-3-methylimidazo[1,2-*a*]pyrazine with 4-(aminomethyl)pyridine. I possessed excellent CDK inhibitory properties, e.g., II demonstrated an IC₅₀ value of 22.5 μ M.

IC ICM C07D487-04

ICS A61K031-495; A61P035-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-605261 [62] WPIX

CROSS REFERENCE: 2004-282837 [26]

DOC. NO. CPI: C2005-182222

TITLE: New pyrazolo(1,5-*a*)pyrimidine compounds useful as cyclin dependent kinase inhibitors and for the treatment of e.g. cancer, inflammation, arthritis, viral diseases.

DERWENT CLASS: B02 B05

INVENTOR(S): ALVAREZ, C S; CHAN, T; DILLARD, L W; DOLL, R J; DWYER, M P; FISCHMANN, T O; GIRIJAVALLABHAN, V M; GUZI, T J; HE, Z M; HOBBS, D W; JAMES, R A; KEERTIKAR, K M; MADISON, V; MALLAMS, A; PARADKAR, V M; PARK, H; PARUCH, K; RIVERA, J; TRAN, V D

PATENT ASSIGNEE(S): (PHAR-N) PHARMACOEPIA DRUG DISCOVERY INC; (SCHE) SCHERING CORP

COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2005077954	A2	20050825	(200562)*	EN	635	C07D487-04	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005077954	A2	WO 2005-US3859	20050208

PRIORITY APPLN. INFO: US 2004-776988 20040211

INT. PATENT CLASSIF.:

MAIN: C07D487-04

SECONDARY: A61K031-495; A61P035-00

BASIC ABSTRACT:

WO2005077954 A UPAB: 20050928

NOVELTY - Pyrazolo(1,5-*a*)pyrimidine compounds, their salts and solvates

are new.

DETAILED DESCRIPTION - Pyrazolo(1,5-a)pyrimidine compounds of formula (I), their salts and solvates are new.

R = e.g. H or optionally substituted (aryl)alkyl, (aryl)alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, alkenylalkyl, alkynylalkyl, heterocyclyl, heterocyclylalkyl or heteroarylalkyl, a group (CHR₅)_n-(hetero)aryl, -(CHR₅)_n-NR₅R₈ or a group of formulae (ia) - (ie);

R₂ = e.g. R₉, alkyl (optionally substituted), CF₃, heterocyclyl, heterocyclylalkyl, halogen, (hetero)aryl (optionally substituted and fused with (hetero)aryl group), (hetero)arylalkyl or a group of formulae (iia)-(iic) (at least one of (hetero)aryl is optionally substituted);

R₃ = e.g. H, halogen, -NR₅R₆, -OR₆, -SR₆, -C(O)N(R₅R₆), (aryl)alkyl, alkynyl, cycloalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl, heterocyclylalkyl or a group of formulae (iiia) - (iiid);

R₄ = H, halo or alkyl;

R₅ = H, aryl or (cyclo)alkyl;

R₆ = e.g. (hetero)aryl, (aryl)alkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, or heteroarylalkyl (all optionally substituted), H or (aryl)alkenyl;

R₁₀ = (aryl)alkyl, (hetero)aryl, cycloalkyl, heterocyclyl, heterocyclylalkyl, or heteroarylalkyl (all optionally substituted) or H;

NR₅+R₁₀, NR₅+R₆ = cycloalkyl or heterocyclyl (optionally substituted by R₉);

R₈ = R₆, -OR₆, -C(O)NR₅R₁₀, -S(O₂)NR₅R₁₀, -C(O)R₇, -C(=N-CN)-NH₂, -C(=NH)-NHR₅, heterocyclyl, or -S(O₂)R₇;

R₉ = halogen, -CN, -NR₅R₁₀, -C(O)R₆, -C(O)NR₅R₁₀, -OR₆, -SR₆, -S(O₂)R₇, -S(O₂)NR₅R₁₀, -N(R₅)S(O₂)R₇, -N(R₅)C(O)R₇ or -N(R₅)C(O)NR₅R₁₀;

m = 0 - 4; and

n, p = 1 - 4.

Full definitions are given in the DEFINITIONS (Full Definitions) field.

INDEPENDENT CLAIMS are also included for:

(A) treating diseases associated with cyclin dependent kinase, by administering (I);

(B) a pharmaceutical composition comprising and at least one carrier and optionally an additional anticancer agent; and

(C) in purified form.

ACTIVITY - Cytostatic; Antiinflammatory; Antiarthritic; Virucide; Neuroprotective; Nootropic; Cardiovascular-Gen.; Fungicide; Immunosuppressive; Ophthalmological; Endocrine-Gen.; Anti-HIV; Dermatological; Nephrotropic; Antirheumatic; Antipsoriatic; Gastrointestinal-Gen.; Antidiabetic; Antiparkinsonian; Muscular-Gen.; Antianemic; Cerebroprotective; Vasotropic; Antiarteriosclerotic; Hepatotropic; Antiarrhythmic; Osteopathic; CNS-Gen.; Respiratory-Gen.; Analgesic.

MECHANISM OF ACTION - Inhibitor of cyclin dependent kinase (CDK) (preferably (CDK2), mitogen activated protein kinase (MAPK/ERK), glycogen synthase kinase 3 (GSK3- beta)); Apoptosis modulator or inhibitor.

CDK2 kinase assays (either cyclin A or E-dependent) were performed in low protein binding 96-well plates. Enzyme was diluted to a final concentration of 50 mu g/ml in kinase buffer containing 50 mM Tris pH 8.0, 10 mM MgCl₂, 1 mM dithiothreitol (DTT), and 0.1 mM sodium orthovanadate. The substrate used in these reactions was a biotinylated peptide derived from Histone H1. The substrate was thawed on ice and diluted to 2 mu M in kinase buffer. 3-Bromo-5-(2-chlorophenyl)-7-(3-pyridylmethylamino)pyrazolo(1,5-a)pyrimidine (IA) was diluted in 10% dimethylsulfoxide (DMSO) to desirable concentrations. For each kinase reaction, the 50 mu g/ml enzyme solution (1 mu g of enzyme) and 20 mu l of the 1 mu M substrate solution were mixed, then combined with 10 ml of diluted compound in each well for testing. The kinase reaction was started

by addition of 50 μ l of 4 μ M ATP and 1 μ Ci of 33 P-ATP. The reaction was allowed to run for 1 hour at room temperature. The reaction was stopped by adding a stop buffer (200 μ l) containing 0.1% Triton X-100 (RTM; surfactant), 1mM ATP, 5mM EDTA, and 5 mg/ml streptavidine coated SPA beads for 15 minutes. The SPA beads were then captured onto a 96-well GF/B filter plate. Non-specific signals were eliminated. The radioactive signal was then measured. (IA) Showed IC50 value of 0.003.

USE - For the treatment of diseases e.g. cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous cell carcinoma; leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphom; acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia; fibrosarcoma, rhabdomyosarcoma; astrocytoma, neuroblastoma, glioma and schwannomas; melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma (claimed). Also for treating inflammation, arthritis, viral diseases, neurodegenerative disease e.g. Alzheimer's disease, cardiovascular diseases and fungal diseases, autoimmune diseases, neurological disease, ocular retinopathy, neuronal disease, alopecia, viral infections, AIDS development in HIV-infected individuals, systemic lupus erythematosus, autoimmune mediated glomerulonephritis, rheumatoid arthritis, psoriasis, inflammatory bowel disease, and autoimmune diabetes mellitus), AIDS-related dementia, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, spinal muscular atrophy and cerebella degeneration, myelodysplastic syndromes, plastic anemia, ischemic injury associated with myocardial infarctions, stroke and reperfusion injury, arrhythmia, atherosclerosis, toxin-induced or alcohol related liver diseases, hematological diseases (e.g. chronic anemia and plastic anemia), degenerative diseases of the musculoskeletal system (e.g. osteoporosis), aspirin-sensitive rhinosinusitis, cystic fibrosis, multiple sclerosis, kidney diseases and cancer pain, HIV and in inhibiting tumor angiogenesis and metastasis. As inhibitors of protein kinases, e.g. protein kinase C, her2, raf 1, MEK1, MAP kinase, epidermal growth factor (EGF) receptor, PDGF receptor, IGF receptor, P13 kinase, weel kinase; Src, Abl.

ADVANTAGE - Compounds (I) inhibit at least one cyclin dependent kinase (CDK) at an activity of 0.0001 - 0.5 (preferably 0.0001 - 0.1) μ M. The compounds may induce or inhibit apoptosis and can modulate the level of cellular RNA and DNA synthesis.

Dwg.0/0

FILE SEGMENT:	CPI
FIELD AVAILABILITY:	AB; GI; DCN
MANUAL CODES:	CPI: B02-D; B02-E; B02-M; B02-T; B04-B03A; B05-A03B; B05-B01J; B06-D08; B06-H; B07-A02B; B07-D01; B07-D11; B07-D12; B07-D13; B08-D02; B10-A09B; B10-A13D; B10-B01; B10-B03B; B10-C02; B14-A02; B14-A02B1; B14-A04; B14-C01; B14-C03; B14-C09; B14-C09B; B14-D06C; B14-E10C1; B14-F01; B14-F02; B14-F03; B14-F05; B14-F07; B14-G01; B14-H01; B14-H01A; B14-H01B; B14-J01; B14-J05; B14-K01; B14-L06; B14-N01A; B14-N03; B14-N04; B14-N10; B14-N12; B14-N16; B14-N17; B14-N17C; B14-R02; B14-S01; B14-S04; B14-S16

TECH

UPTX: 20050928

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (disclosed):

Preparation of (I) involves:

(A) condensation of a pyridones compound of formula $R^3-C(=O)-CH(R^4)-C(=O)-O-$ with an amine derivative of formula (II) using AcOH under reflux

condition to obtain a pyridone derivative of formula (III);
 (B) treating (III) with POCl_3 to obtain a chloride of formula (IV); and
 (C) introducing the N7-amino functionality through displacement of the chloride of formula (IV) by reaction with an amine of formula $\text{R-CH(R}_5\text{)-NH}_2$ in the presence of potassium carbonate and CH_3CN .

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method also involves administration of at least one second compound (preferably an anti-cancer agent) and further involves radiation therapy.
 Preferred Components: The anti-cancer agent is a cytostatic agent, cisplatin, doxorubicin, taxotere, taxol, etoposide, CPT-11 (RTM), irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methotrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336 (RTM), R115777 (RTM), L778123 (RTM), BMS 214662 (RTM), Iressa, Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan, gemcitabine, Uracil mustard, Chloromethine, Ifosfamide, Melphalan, Chlorambucil, Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan, Carmustine, Lomustine, Streptozocin, Dacarbazine, Floxuridine, Cytarabine, 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, oxaliplatin, leucovirin, ELOXATIN (RTM), Pentostatine, Vinblastine, Vincristine, Vindesine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mithramycin, Deoxycoformycin, Mitomycin-C, L-Asparaginase, Teniposide, 17alpha-Ethinylestradiol, Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone, Dromostanolone propionate, Testolactone, Megestrolacetate, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene, Hydroxyprogesterone, Aminoglutethimide, Estramustine, Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin, Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane, Mitoxantrone, Levamisole, Navelbine, Anastrozole, Letrazole, Capecitabine, Reloxafine, Droloxafine, or Hexamethylmelamine.

L20 ANSWER 12 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2005-616512 [63] WPIX
 DOC. NO. CPI: C2005-185499
 TITLE: New pyrazolo(1,5-a)triazine derivatives useful for treating e.g. viral infections, leukemia, cancer and Kaposi's sarcoma.
 DERWENT CLASS: B02 B05
 INVENTOR(S): GUZI, T J; PARUCH, K
 PATENT ASSIGNEE(S): (SCHE) SCHERING CORP
 COUNTRY COUNT: 109
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
US 2005187219	A1	20050825	(200563)*		45	A61K031-53	
WO 2005082908	A1	20050909	(200563)	EN		C07D487-04	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT							
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ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE							
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG							
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ							
OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA							
UG US UZ VC VN YU ZA ZM ZW							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
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US 2005187219 A1 Provisional US 2004-547685P 20040225
US 2005-64044 20050223
WO 2005082908 A1 WO 2005-US5614 20050223

PRIORITY APPLN. INFO: US 2004-547685P 20040225; US
2005-64044 20050223

INT. PATENT CLASSIF.:

MAIN: A61K031-53; C07D487-04
SECONDARY: A61P035-00

BASIC ABSTRACT:

US2005187219 A UPAB: 20051003

NOVELTY - Pyrazolo(1,5-a)triazine derivatives (I), their salts, solvates or esters are new.

DETAILED DESCRIPTION - Pyrazolo(1,5-a)triazine derivatives of formula (I), their salts, solvates or esters are new.

R1 = (cyclo)alkyl, (hetero)aryl, heteroarylalkyl, arylalkyl, or cycloalkylalkyl (all optionally substituted with T, (hetero)aryl or heterocyclyl), H or NR6R7;

R2 = (cyclo)alkyl, alkenyl, alkynyl, trifluoromethyl, -OR7, -SR7, hydroxyalkyl, haloalkyl, halo, CN, (hetero)aryl, formyl, nitro, (hetero)aralkylcarbonyl, alkylcarbonyl or -alkylene-N(R8R9);

R8, R9 = H or alkyl;

NR8R9 = a 5-7 membered heterocycle;

R3 = piperidinyl, pyrrolidinyl (both substituted n times by R10), piperazinyl (substituted at 4-position by R5 and at other positions n times by R10), N-containing heterocycle of formula (i), -NR4R5, H, alkyl, (ar)alkylthio, alkylsulfinyl or aralkylsulfinyl;

R4 = (cyclo)alkyl or heterocyclyl (both optionally mono- to tetra-substituted with T, hydroxymethyl, hydroxyethyl or hydroxypropyl);

R6 = H, alkyl or aryl;

R7 = H or alkyl;

R10 = T or hydroxyalkyl;

T = halo, alkyl, trifluoromethyl, OR6, NR6R7, SR6, SO2R6, CN, SO2N(R6R7) or NO2;

R5 = H, alkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, heterocyclyl, acyl or heteroarylalkyl; and

n = 0 - 4.

Provided that

(1) when R2 is 1-4C alkyl and R5 is H, then R4 is other than 1-4C alkyl;

(2) when R2 is halo, CN, formyl, nitro, alkylcarbonyl, (hetero)aralkylcarbonyl or -alkylene-N(R8R9), then R3 is other than H, (ar)alkylthio, (ar)alkylsulfinyl or -NR4R5 and n is other than 0; and

(3) when R2 is (cyclo)alkyl, alkenyl or alkynyl, then R3 is other than NH(methyl), N,N(dimethyl), NH(acetyl) or N(methyl)(acetyl).

INDEPENDENT CLAIMS are included for the following:

(1) treating at least one disease associated with **kinase** involving administering to mammal, (I) and at least one anti-cancer agent; and

(2) a pharmaceutical composition (c1) comprising (I) and at least one carrier.

ACTIVITY - Cytostatic; Anti-HIV; Virucide; Antiinflammatory; Dermatological; Immunosuppressive; Nephrotropic; Antiarthritic; Antirheumatic; Antipsoriatic; Gastrointestinal-Gen.; Antidiabetic; Neuroprotective; Nootropic; Antiparkinsonian; Antianemic; Cardiant; Cerebroprotective; Antiarrhythmic; Antiarteriosclerotic; CNS-Gen.; Respiratory-Gen.; Osteopathic; Analgesic.

MECHANISM OF ACTION - Protein Kinase (preferably cyclin

dependent **kinase-1** (CDK1) CDK2, CDK3, CDK4 or CDK5; mitogen activated protein **kinase** (MAPK/ERK) or glycogen synthase **kinase 3** (GSK3 beta), checkpoint **kinase-1** (CHK-1), CHK-2, Aurora A - C, AKT1, AKT2 or AKT3) inhibitor; Apoptosis modulator. **Kinase** activity was determined by performing in vitro CDK2 **kinase** assay (either cyclin A or E dependent) using 5-((8-ethyl-2-((S)-2-(2-hydroxy-ethyl)-piperidin-1-yl)-pyrazolo(1,5-a)(1,3,5)triazin-4-ylamino)methyl)-1-methyl-1H-pyridin-2-one (Ia). Recombinant baculoviruses expressing cyclins A, E and CDK2 are infected into SF9 cells. IC50 value of (Ia) was 0.00048 μ M.

USE - For inhibiting at least one **kinase**; or treating at least one disease (e.g. cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin including squamous cell carcinoma; leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, beta -cell lymphoma, T-cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma; acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia; fibrosarcoma, rhabdomyosarcoma; astrocytoma, neuroblastoma, glioma and schwannomas; melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma) associated with the **kinase** (claimed); also for treatment of viral infections (including but not limited to herpevirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus), prevention of AIDS development in HIV-infected individuals, autoimmune diseases (including systemic lupus erythematosus, autoimmune mediated glomerulonephritis, rheumatoid arthritis, psoriasis, inflammatory bowel disease, and autoimmune diabetes mellitus), neurodegenerative disorders (including Alzheimer's disease, AIDS-related dementia, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, spinal muscular atrophy and cerebellar degeneration), myelodysplastic syndromes, aplastic anemia, ischemic injury associated with myocardial infarctions, stroke and reperfusion injury, arrhythmia, atherosclerosis, toxin-induced or alcohol related liver diseases, hematological diseases (including chronic anemia and aplastic anemia), degenerative diseases of the musculoskeletal system (including osteoporosis and arthritis) aspirin-sensitive rhinosinusitis, cystic fibrosis, multiple sclerosis, kidney diseases and cancer pain.

ADVANTAGE - The pyrazolo(1,5-a)triazine derivatives are excellent CDK2 inhibitors.

Dwg.0/0

FILE SEGMENT:	CPI
FIELD AVAILABILITY:	AB; GI; DCN
MANUAL CODES:	CPI: B01-A02; B01-B01; B01-B02; B01-B03; B01-C03; B01-C05; B02-B; B02-D; B02-M; B02-S; B04-B03A; B04-B03B; B04-B03D; B04-C01B; B04-N04; B05-A03B; B05-B01J; B06-H; B07-H; B10-A03; B10-A09B; B10-A13D; B10-A19; B10-B01A; B10-B02A; B10-B03B; B10-B04B; B10-D03; B10-E02; B10-H01; B14-A02; B14-C01; B14-C09; B14-D06C; B14-E10C1; B14-F01A; B14-F01E; B14-F02D1; B14-F03; B14-F05; B14-F07; B14-G02D; B14-H01; B14-J01; B14-J05; B14-K01; B14-N01A; B14-N03; B14-N04; B14-N10; B14-N12; B14-N16; B14-N17; B14-S01; B14-S04; B14-S16

TECH UPTX: 20051003

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) involves:

(1) acylation of 2H-pyrazol-3-ylamine (substituted at 4 position by R2) using ethoxycarbonyl isothiocyanate followed by sodium hydroxide catalyzed cyclization to give thione of formula (ii);

(2) methylation of (ii) using methyl iodide followed by chlorination using phosphorusoxytrichloride to give a thioether of formula (iii); and
 (3) displacement of (iii) with an amine of formula R_1NH_2 to give (I)
 (where R_3 is SCH_3).

$R=R_1$.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method further involves radiation therapy. Preferred Composition: The (c1) additionally comprises at least one anti-cancer agent. Preferred Components: The anti-cancer-agent is selected from a cytostatic agent, cisplatin, doxorubicin, taxotere, taxol, etoposide, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methotrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, Iressa, Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan, gemcitabine, Uracil mustard, Chloromethine, Ifosfamide, Melphalan, Chlorambucil, Triethylenemelamine, Busulfan, Pipobroman, Triethylenethiophosphoramine, Carmustine, Lomustine, Streptozocin, Dacarbazine, Floxuridine, Cytarabine, 6-Thioguanine, 6-Mercaptopurine, Fludarabine phosphate, oxaliplatin, leucovirin, ELOXATIN (RTM; anti-cancer agent), Pentostatine, Vindesine, Vinblastine, Vincristine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mithramycin, Deoxycoformycin, Mitomycin-C, L-Asparaginase, Teniposide, 17alpha-ethinylestradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, dromostanolone propionate, testolactone, megestrolacetate, CPT-11, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, hydroxyprogesterone, aminoglutethimide, Navelbene, Estramustine, Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin, Carboplatin, hydroxyurea, Procarbazine, Amsacrine, Mitotane, Mitoxantrone, Levamisole, Anastrozole, Letrazole, Capecitabine, Reloxafine, Droloxafine or Hexamethylmelamine.

L20 ANSWER 13 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2005-434419 [44] WPIX
 CROSS REFERENCE: 2004-294420 [27]
 DOC. NO. CPI: C2005-133334
 TITLE: New imidazopyrazine derivatives are cyclin dependent kinase inhibitors useful to treat cancers of e.g. bladder, breast, colon, kidney, liver, lung, esophagus, gall bladder and ovary.
 DERWENT CLASS: B02 B05
 INVENTOR(S): DOLL, R J; DWYER, M P;
 GIRIJAVALLABHAN, V M; GUZI, T J;
 MALLAMS, A; PARUCH, K
 PATENT ASSIGNEE(S): (DOLL-I) DOLL R J; (DWYE-I) DWYER M P; (GIRI-I) GIRIJAVALLABHAN V M; (GUZI-I) GUZI T J; (MALL-I) MALLAMS A; (PARU-I) PARUCH K
 COUNTRY COUNT: 1
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
US 2005130980	A1	20050616	(200544)*		54	A61K031-498	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005130980	A1 Provisional	US 2002-412997P	20020923
	Div ex	US 2003-665005	20030919
		US 2005-47524	20050131

PRIORITY APPLN. INFO: US 2002-412997P 20020923; US
2003-665005 20030919; US
2005-47524 20050131

INT. PATENT CLASSIF.:

MAIN: A61K031-498
SECONDARY: C07D487-04

BASIC ABSTRACT:

US2005130980 A UPAB: 20050712

NOVELTY - **Imidazopyrazine** derivatives (I) are new.

DETAILED DESCRIPTION - **Imidazopyrazine** derivatives of formula (I) are new.

R = aryl, heteroaryl, cycloalkyl, arylalkyl, alkenyl or heterocyclyl (all optionally substituted), H, halo, heterocyclylalkyl, alkynyl, C(O)R7 or a group of formula (i)-(iv) (all optionally substituted by at least 1 halo, alkyl, cycloalkyl, CF3, CN, OCF3, OR6, C(O)R7, NR5R6, C(O2)R6, C(O)NR5R6, (CHR5)nOR6, SR6, S(O2)R7, S(O2)NR5R6, N(R5)S(O2)R7, N(R5)C(O)R7 or N(R5)C(O)NR5R6), H or halo;

R1 = H, halo or alkyl;

R2 = alkyl;

R3 = aryl, heteroaryl or heterocyclyl (all optionally substituted by at least 1 S(O2)R6 or T), (CHR5)n-aryl, (CHR5)nheteroaryl, (CHR5)n-OR, S(O2)R6, C(O)R6, S(O2)NR5R6, C(O)OR6, C(O)NR5R6, cycloalkyl, CH(aryl)2, (CH2)m-NR8, (CHR5)n-CH(aryl)2, a group of formula (v) or (vi) or H;

T = halo, aryl, alkyl, cycloalkyl, CF3, CN, OCF3, OR5, NR5R6, C(O2)R5, C(O)NR5R6, SR6, S(O2)NR5R6, N(R5)S(O2)R7, N(R5)C(O)R7 or N(R5)C(O)NR5R6;

R5 = H or alkyl;

R6 = alkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl (all optionally substituted by at least 1 CH2OR5, S(O2)R7 or T) or H;

R7 = alkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl (all optionally substituted by at least 1 CH2OR5, S(O2)R7 or T);

R8 = R6, C(O)NR5R6, S(O2)NR5R6, C(O)R7, C(O2)R6, S(O2)R7 or (CH2)-aryl;

R9 = halo, CN, NR5R6, C(O2)R6, C(O)NR5R6, OR6, C(O)R7, SR6, S(O2)R7, S(O2)NR5R6, N(R5)S(O2)R7, N(R5)C(O)R7 or N(R5)C(O)NR5R6;

m = 0-4;

n = 1-4, and

p = 0-3.

An INDEPENDENT CLAIM is also included for treating cyclin dependent kinase mediated diseases which comprises administering (I) and optionally a second compound (anticancer agent).

ACTIVITY - Cytostatic; Anti-HIV.

MECHANISM OF ACTION - Cyclin dependent kinase-2 inhibitor.

In an in vitro assay used for determining cyclin dependent kinase-2 inhibitory activity, results showed that (3-methylimidazo(1,2- α)pyrazin-8-yl)-phenylamine (Ia) exhibited an IC50 value of 15 μ M.

USE - Used to treat cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate and skin, squamous cell carcinoma, leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma, Burkett's lymphoma, acute and chronic myelogenous leukemia, myelodysplastic syndrome, promyelocytic leukemia, fibrosarcoma, rhabdomyosarcoma, astrocytoma, neuroblastoma, glioma, schwannomas, melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma (claimed).

Dwg.0/0
 FILE SEGMENT: CPI
 FIELD AVAILABILITY: AB; GI; DCN
 MANUAL CODES: CPI: B04-B03A; B05-A03B; B05-B01J; B06-A03; B06-D07;
 B06-D08; B06-D13; B06-E05; B07-B01; B07-D11;
 B07-D12; B07-D13; B10-B04B; B14-D06C; B14-H01

TECH UPTX: 20050712

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: None given.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: Treating cyclin dependent **kinase** mediated disease further comprises radiation therapy. (I) is in purified form and the cyclin dependent **kinase** inhibitor is mitogen activated protein **kinase** (MAPK/ERK) and glycogen synthase **kinase**-3beta

Preferred Compounds: The anticancer agent is cytostatic agent, taxotere, taxol, etoposide, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methotrexate, temozolomide, cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, iressa, tarceva, antibodies to epidermal growth factor receptor, glaive, intone, are-C, adriamycin, cytoxan, gemcitabine, uracil mustard, chlormethine, ifosfamide, melphalan, chlorambucil, pipobroman, triethylenemelamine, triethylenethiophosphoramine, busulfan, carmustine, lomustine, streptozocin, dacarbazine, floxuridine, cytarabine, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, oxaliplatin, leucovorin, pentostatine, vinblastine, vincristine, vindesine, bleomycin, dactinomycin, daunorubicin, doxorubicin, epirubicin, idarubicin, mithramycin, deoxycoformycin, mitomycin-C, L-asparaginase, teniposide 17a-ethinylestradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, dromostanolone propionate, testolactone, megesterolacetate, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesteroneacetate, leuprolide, flutamide, toremifene, goserelin, cisplatin, carboplatin, hydroxyurea, amsacrine, procarbazine, mitotane, mitoxantrone, levamisole, navelbene, anastrozole, letrozole, capecitabine, reloxafine, droloxafine or hexamethylmelamine.

L20 ANSWER 14 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2004-294420 [27] WPIX
 CROSS REFERENCE: 2005-434419 [44]
 DOC. NO. CPI: C2004-112619
 TITLE: New imidazo(1,2-a)**pyrazine** compounds useful for treating e.g. keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma.
 DERWENT CLASS: B02
 INVENTOR(S): DOLL, R J; DWYER, M P;
 GIRIJAVALLABHAN, V M; GUZI, T J;
 MALLAMS, A K; PARUCH, K; GIRIJAVALLABHAN, V M &; MALLAMS, A
 PATENT ASSIGNEE(S): (SCHE) SCHERING CORP
 COUNTRY COUNT: 105
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
US 2004063715	A1	20040401	(200427)*		60	A61K031-498	
WO 2004026877	A1	20040401	(200431)	EN		C07D487-04	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS							
LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM							
DZ EC EE EG ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR							

LT LU LV MA MD MG MK MN MX MZ NI NO NZ PG PH PL PT RO RU SC SE SG
 SK SL SY TJ TM TN TR TT TZ UA UZ VC VN YU ZA ZM
 AU 2003272476 A1 20040408 (200462) C07D487-04
 EP 1543008 A1 20050622 (200541) EN C07D487-04
 R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
 MC MK NL PT RO SE SI SK TR
 US 6919341 B2 20050719 (200547) C07D487-04
 TW 2004013378 A 20040801 (200581) C07D487-04
 CN 1694886 A 20051109 (200618) C07D487-04
 JP 2006507253 W 20060302 (200621) 69 C07D487-00
 MX 2005003120 A1 20050701 (200628) A61K031-495
 ZA 2005002375 A 20051130 (200628) 96 C07D000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004063715	A1 Provisional	US 2002-412997P	20020923
		US 2003-665005	20030919
WO 2004026877	A1	WO 2003-US29209	20030919
AU 2003272476	A1	AU 2003-272476	20030919
EP 1543008	A1	EP 2003-754658	20030919
		WO 2003-US29209	20030919
US 6919341	B2 Provisional	US 2002-412997P	20020923
		US 2003-665005	20030919
TW 2004013378	A	TW 2003-125979	20030919
CN 1694886	A	CN 2003-825177	20030919
JP 2006507253	W	WO 2003-US29209	20030919
		JP 2004-537904	20030919
MX 2005003120	A1	WO 2003-US29209	20030912
		MX 2005-3120	20050322
ZA 2005002375	A	ZA 2005-2375	20050322

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003272476	A1 Based on	WO 2004026877
EP 1543008	A1 Based on	WO 2004026877
JP 2006507253	W Based on	WO 2004026877
MX 2005003120	A1 Based on	WO 2004026877

PRIORITY APPLN. INFO: US 2002-412997P 20020923; US
 2003-665005 20030919

INT. PATENT CLASSIF.:

MAIN: A61K031-495; A61K031-498; C07D000-00; C07D487-00;
 C07D487-04
 SECONDARY: A61K031-4985; A61K045-00; A61P035-00; A61P035-02;
 A61P043-00

BASIC ABSTRACT:

US2004063715 A UPAB: 20060502

NOVELTY - Imidazo(1,2-a)pyrazine compounds are new.

DETAILED DESCRIPTION - Imidazo(1,2-a)pyrazine compounds of
 formula (I) are new.

R = (hetero)aryl, cycloalkyl, arylalkyl, heterocyclyl, alkenyl, T1
 (all optionally substituted by U1), alkynyl, -C(O)R7, H, halo or
 heterocyclylalkyl;

T1 = piperazin-1-yl, pyrrolidin-1-yl, piperidine-1-yl,
 pyrrolidin-3-yl, piperidine-4-yl, piperidine-3-yl, azepan-4-yl,
 pyrrolidin-2-yl or piperidine-2-yl (all substituted by (R8)n);

U1 = U2 or -(CHR5)nOR6;
 U2 = halo, (cyclo)alkyl, CF3, CN, -OCF3, -OR6, -C(O)R7, -NR5R6, -C(O)2R6, -C(O)NR5R6, -SR6, -S(O)2R7, -S(O)2NR5R6, -N(R5)S(O)2R7, -N(R5)C(O)R7 or -N(R5)C(O)NR5R6;
 R1 = H, halo or alkyl;
 R2 = (hetero)aryl, arylalkyl or heterocyclyl (all optionally substituted by U2), halo, R9, alkyl (optionally mono- - hexa-substituted by R9), heteroarylalkyl, alkenyl, alkynyl, -CF3, -C(O)R7, T2 or cycloalkyl;
 T2 = -(CH2)m-piperazin-1-yl(substituted at position 4 by R8), -(CH2)m-piperidine(substituted at position 1 by R8), -aryl-piperazin-1-yl(substituted at position 4 by R8) or -aryl-piperidine(substituted at position 1 by R8);
 R3 = (hetero)aryl, -(CHR5)n-(hetero)aryl or heterocyclyl (all optionally substituted by U3), H, -(CHR5)n-OR6, -S(O)2R5, -C(O)R6, -S(O)2NR5R6, -C(O)OR6, -C(O)NR5R6, cycloalkyl, -CH(aryl)2, -(CH2)m-NR8, -(CHR5)n-CH(aryl)2, -(CHR5)n-pyrrolidin-2-on-1-yl or -(CH2)m-piperidine(substituted at position 1 by R8);
 U3 = halo, alkyl, aryl, cycloalkyl, CF3, CN, -OCF3, -OR5, -NR5R6, -C(O)2R5, -C(O)NR5R6, -SR6, -S(O)2R6, -S(O)2NR5R6, -N(R5)S(O)2R7, -N(R5)C(O)R7 or -N(R5)C(O)NR5R6;
 R5 = H or alkyl;
 R7 = alkyl, heteroarylalkyl, (hetero)aryl or arylalkyl (all optionally substituted by U4);
 U4 = halo, alkyl, aryl, cycloalkyl, CF3, CN, -OCF3, -OR5, -NR5R6, -CH2OR5, -C(O)2R5, -C(O)NR5R6, -SR6, -S(O)2R7, -S(O)2NR5R6, -N(R5)S(O)2R7, -N(R5)C(O)R7 or -N(R5)C(O)NR5R6;
 R6 = H or R7;
 R8 = R6, -C(O)NR5R6, -S(O)2NR5R6, -C(O)R7, -C(O)2R6, -S(O)2R7 or -(CH2)-aryl;
 R9 = halo, CN, NR5R6, -C(O)2R6, -C(O)NR5R6, -OR6, -N(R5)S(O)2R7, -N(R5)C(O)R7 or -N(R5)C(O)NR5R6;
 m = 0 - 4;
 n = 1 - 4; and
 p = 0 - 3.

An INDEPENDENT CLAIM is included for treating disease associated with cyclin dependent **kinase** involving administering to a mammal (I), its salt or solvate, and an anti-cancer agent; and optionally performing radiation therapy.

ACTIVITY - Cytostatic; Anti-HIV; Antithyroid; Antiinflammatory; Antiarthritic; Virucide; Nootropic; Neuroprotective; Fungicide; Cardiovascular-Gen.

MECHANISM OF ACTION - Cyclin dependent **kinases** (CDKs) (preferably CDK1, CDK2, CDK4 - CDK8 mitogen activated protein **kinase** (MAPK/ERK), glycogen synthase **kinase** 3 (GSK3 beta)) inhibitor; Protein **kinase** (preferably protein **kinase** C, her2, raf1, MEK1, MAP **kinase**, EGF receptor, PDGF receptor, IGF receptor, P13 **kinase**, weel **kinase**, Src and Abl) inhibitor; Apoptosis inhibitor; Tumor angiogenesis inhibitor; Metastasis inhibitor. An in vitro CDK2 **kinase** assay was performed in low protein binding 96-well plates. Enzyme was diluted to a final concentration of 50 micro g/ml in **kinase** buffer containing Tris pH 8 (50 mM), magnesium chloride (10 mM), dithiothreitol and sodium orthovanadate (0.1 mM). A biotinylated peptide derived from Histone H1 was thawed on ice and diluted to 2 micro M in **kinase** buffer. 2-(3-Bromo-6-(2-chloro-phenyl)-imidazo(1,2-a)**pyrazin**-8-ylamino)-propan-1-ol (A) was diluted in 10% dimethylsulfoxide. Enzyme solution (20 micro l) and substrate solution (20 micro l) were mixed, then combined with diluted compound (10 micro l) in each well for testing. The **kinase** reaction was started by adding ATP (50 micro l) and 33P-ATP

(1 micro Ci) and allowed to run for 1 hour at room temperature. The reaction was stopped. The SPA beads were captured and after work up, IC50 value was determined which was found to be 0.2 micro M.

USE - For treating disease associated with cyclin dependent kinase including cancer (of bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate and skin) e.g. squamous cell carcinoma; leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma; acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia; fibrosarcoma, rhabdomyosarcoma; astrocytoma, neuroblastoma, glioma and schwannomas; melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma in a mammal (all claimed). Also useful for treating inflammation, arthritis, viral disease, neurodegenerative diseases (e.g. Alzheimer's disease), cardiovascular disease and fungal disease.

ADVANTAGE - The compounds are potent inhibitors of cyclin dependent kinases.

Dwg.0/0

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: B01-B02; B01-C05; B02-D; B02-E; B02-M; B04-B03A; B04-C01B; B05-A03B; B05-B01J; B05-B01M; B05-C05; B06-H; B07-H; B10-A10; B10-A13B; B10-A19; B10-B02E; B10-B03; B10-B04A; B10-B04B; B10-E02; B14-A02; B14-A04; B14-C03; B14-C09; B14-D06; B14-F01; B14-H01; B14-H04; B14-J01A4; B14-L06; B14-N01; B14-N10; B14-N11; B14-N12; B14-N13; B14-N14

TECH UPTX: 20040426

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No general preparation given.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Agent: The anti-cancer agent is cytostatic agent, cisplatin, doxorubicin, taxotere, taxol, etoposide, CPT-11 (RTM; topoisomerase I inhibitor), irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methotrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336 (RTM), R115777 (RTM; tipifarnib), L778123 (RTM; farnesyl protein transferase inhibitor), BMS 214662 (RTM; farnesyl protein transferase inhibitor), iressa, tarceva, antibodies to EGFR, gleevec, intron, ara-C, adriamycin, cytoxan, gemcitabine, uracil mustard, chlormethine, ifosfamide, melphalan, chlorambucil, pipobroman, triethylenemelamine, triethylenethiophosphoramine, busulfan, carmustine, lomustine, Streptozocin, Dacarbazine, Floxuridine, Cytarabine, 6-Mercaptopurine, 6-thioguanine, fludarabine phosphate, oxaliplatin, leucovirin, ELOXATIN (RTM; oxaliplatin), pentostatin, vinblastine, vincristine, vindesine, bleomycin, dactinomycin, daunorubicin, doxorubicin, epirubicin, idarubicin, mithramycin, deoxycoformycin, mitomycin-C, L-asparaginase, teniposide 17alpha-ethinyloestradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, dromostanolone propionate, testosterone, megestrolacetate, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesteroneacetate, leuprolide, flutamide, toremifene, goserelin, cisplatin, carboplatin, hydroxyurea, amsacrine, procarbazine, mitotane, mitoxantrone, levamisole, navelbine, anastrozole, letrozole, capecitabine, reloxafine, droloxafine or hexamethylmelamine.

L20 ANSWER 15 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-679276 [64] WPIX

Searched by Barb O'Bryen, STIC 2-2518

DOC. NO. CPI: C2003-185547
 TITLE: New 3,4-disubstituted pyridazinedione compounds useful for the treatment of e.g. psoriasis, atopic dermatitis, asthma, chronic obstructive pulmonary disease, adult respiratory disease or arthritis.
 DERWENT CLASS: B02 B03
 INVENTOR(S): BALDWIN, J J; CHAO, J; DWYER, M; LI, G; MERRITT, R J; TAVERAS, A G; YU, Y; MERRITT, J R
 PATENT ASSIGNEE(S): (PHAR-N) PHARMA COPEIA INC; (SCHE) SCHERING CORP; (PHAR-N) PHARMA COPEIA DRUG DISCOVERY INC
 COUNTRY COUNT: 100
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2003057676	A1	20030717	(200364)*	EN	210	C07D237-22	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS							
LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM							
DZ EC EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT							
LU LV MA MD MG MK MN MX MZ NO NZ PH PL PT RO RU SC SE SG SK SL TJ							
TM TN TR TT TZ UA UZ VC VN YU ZA ZM							
AU 2003207460	A1	20030724	(200421)			C07D237-22	
US 2004063709	A1	20040401	(200425)			A61K031-501	
EP 1461321	A1	20040929	(200463)	EN		C07D237-22	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV							
MC MK NL PT RO SE SI SK TR							
US 6878709	B2	20050412	(200525)			A61K031-50	
CN 1582280	A	20050216	(200535)			C07D237-22	
JP 2005516029	W	20050602	(200541)		187	C07D237-22	
MX 2004006555	A1	20041101	(200558)			A61K031-501	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003057676	A1	WO 2003-US299	20030103
AU 2003207460	A1	AU 2003-207460	20030103
US 2004063709	A1 Provisional	US 2002-346248P	20020104
		US 2003-335789	20030102
EP 1461321	A1	EP 2003-705667	20030103
		WO 2003-US299	20030103
US 6878709	B2 Provisional	US 2002-346248P	20020104
		US 2003-335789	20030102
CN 1582280	A	CN 2003-801923	20030103
JP 2005516029	W	JP 2003-557993	20030103
		WO 2003-US299	20030103
MX 2004006555	A1	WO 2003-US299	20030103
		MX 2004-6555	20040702

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003207460	A1 Based on	WO 2003057676
EP 1461321	A1 Based on	WO 2003057676
JP 2005516029	W Based on	WO 2003057676
MX 2004006555	A1 Based on	WO 2003057676

PRIORITY APPLN. INFO: US 2003-335789 20030102; US

2002-346248P 20020104

INT. PATENT CLASSIF.:

MAIN: A61K031-50; A61K031-501; C07D237-22
SECONDARY: A61K031-5011; A61K031-506; A61K031-5377; A61K045-00;
A61P001-02; A61P001-04; A61P007-02; A61P009-00;
A61P009-10; A61P009-14; A61P011-00; A61P011-06;
A61P013-12; A61P017-00; A61P017-06; A61P019-02;
A61P025-28; A61P027-02; A61P031-04; A61P031-12;
A61P031-14; A61P031-18; A61P031-20; A61P031-22;
A61P033-06; A61P035-00; A61P035-000; A61P037-02;
A61P037-04; A61P039-00; A61P043-00; C07D401-12;
C07D403-02; C07D403-12; C07D403-122; C07D405-12;
C07D405-122; C07D409-12; C07D409-122; C07D409-14;
C07D413-02; C07D417-02; C07D417-12; C07D417-122

BASIC ABSTRACT:

WO2003057676 A UPAB: 20031006

NOVELTY - 3,4-Disubstituted pyridazinedione compounds (I) are new.

DETAILED DESCRIPTION - 3,4-Disubstituted pyridazinedione compounds (I), their salts or solvates are new.

R1, R15 = e.g. (hetero)aryl, alkyl or H;

A = e.g. group formula (ia);

B' = e.g. phenyl (substituted by R2, R3, R4, R5 and R6 at positions 2, 3, 4, 5 and 6 respectively) or 1 H-benzotriazol-7-yl (substituted by R4, R5, R6 at positions 4, 5 and 6 respectively);

R2 = e.g. H, OH, C(O)OH, SH;

R5, R6 = e.g. H, halo, alkyl;

R3, R4 = e.g. OH or R5;

R8 = e.g. alkyl, (hetero)aryl or (hetero)arylalkyl;

R9 = e.g. halo or -CF₃;

m = 1 - 5;

X = not defined; and

p = 0 - 4.

Full definitions are given in the DEFINITIONS (Full Definitions) section.

ACTIVITY - Antipsoriatic; Dermatological; Antiasthmatic; Respiratory; Antiarthritic; Antiinflammatory; Gastrointestinal; Antiulcer; Antibacterial; Immunosuppressive; Cerebroprotective; Vasotropic; Nephrotropic; Thrombolytic; Nootropic; Neuroprotective; Protozoacide; Antiarteriosclerotic; Cardiant; Cytostatic; Virucide; Hepatotropic; Anti-HIV; Ophthalmological; Antidiabetic.

MECHANISM OF ACTION - CXC-chemokine receptor (preferably CXCR2 and CXCR1 receptor) antagonist; Angiogenesis inhibitor; Interleukin (IL)-8 receptor binding inhibitor.

Test details are described but no results for the specific compounds are given. In general, the compounds showed IC₅₀ value of 1 - 10000 nM.

USE - In the manufacture of a medicament for the treatment of a chemokine-mediated disease including psoriasis, atopic dermatitis, asthma, chronic obstructive pulmonary disease, adult respiratory disease, arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, stroke, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, Alzheimer's disease, graft versus host reaction, allograft rejection, malaria, acute respiratory distress syndrome, delayed type hypersensitivity reaction, atherosclerosis and cerebral and cardiac ischemia; for the treatment of cancer (e.g. melanoma, gastric carcinoma or non-small cell lung carcinoma), gingivitis, respiratory virus, herpes virus, hepatitis virus, HIV, Kaposi's sarcoma associated virus and angiogenic ocular disease (e.g. ocular inflammation, retinopathy of prematurity, diabetic retinopathy, macular degeneration with the wet type preferred and corneal neovascularization (all claimed).

The ocular inflammation includes uveitis.

ADVANTAGE - (I) modulate activity at CXC-chemokine receptors by increasing IL-8 production, which is responsible for chemotaxis of neutrophil and T-cell subsets into the inflammatory site and growth of tumors.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B05-B01B; B07-D10; B14-A01; B14-A02; B14-A03;
B14-C03; B14-C09; B14-E08; B14-E10; B14-F01;
B14-F04; B14-F07; B14-F09; B14-G02; B14-H01;
B14-J01A4; B14-K01; B14-L07; B14-N03; B14-N16;
B14-N17; B14-S04

TECH UPTX: 20031006

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Dibromomaleic anhydride is condensed with a optionally substituted hydrazine of formula R1-NH-NH-R15 in the presence of aqueous H2SO4 to give a cyclic hydrazide derivative of formula (i). The condensation of (i) with one equivalent of an amine ANH2 gives a cyclic hydrazine derivative of formula (ii) followed by adding a second amine B'NH2 to give (I).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Medicament: The medicament further comprises at least one anti-cancer agent and/or radiation therapy (preferably alkylating agent, antimetabolite, natural product or its derivative, hormone, anti-hormone, anti-angiogenic agent, steroid (e.g. synthetic analog) or synthetic) or anti-angiogenesis compound. The anti-angiogenic agent is marimastat, AG3340, Col-3, neovastat, BMS-275291, thalidomide, squalamine, endostatin, SU-5416, SU-6668, interferon-alpha, anti-VEGF antibody, EMD121974, CAI, interleukin-12, IM862, platelet factor-4, vitaxin, angiostatin, suramin, TNP-470, PTK-787, ZD-6474, ZD-101, Bay 129566, CGS27023A, VEGF receptor kinase inhibitor, docetaxel or paclitaxel.

L20 ANSWER 16 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-468193 [44] WPIX
DOC. NO. CPI: C2003-124782
TITLE: New 3,4-disubstituted maleimide compounds useful for treating chemokine mediated disease e.g. psoriasis, stroke, asthma, and cancer.
DERWENT CLASS: B02 B03 B05 D16
INVENTOR(S): BALDWIN, J J; CHAO, J; DWYER, M; FERREIRA, J A; GIRIJAVALLABHAN, V M; LI, G; MERRITT, J R; TAVERAS, A G; DWYNER, M; MERRIT, J R
PATENT ASSIGNEE(S): (PHAR-N) PHARMACOEPIA INC; (SCHE) SCHERING CORP; (PHAR-N) PHARMACOEPIA DRUG DISCOVERY INC
COUNTRY COUNT: 99
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2003031440	A1	20030417	(200344)*	EN	115	C07D409-12	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM DZ EC EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX MZ NO NZ PH PL PT RO RU SE SG SI SK SL TJ TM TN TR TT TZ UA UZ VC VN YU ZA ZM							
US 2004034229	A1	20040219	(200414)			C07D417-14	
EP 1434775	A1	20040707	(200444)	EN		C07D409-12	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC							

	MK	NL	PT	RO	SE	SI	SK	TR	
AU	2002351478			A1	20030422			(200461)	C07D409-12
JP	2005505595			W	20050224			(200516)	434 C07D207-456
US	6903131			B2	20050607			(200538)	A61K031-4015
CN	1599734			A	20050323			(200545)	C07D409-12
MX	2004003439			A1	20040701			(200545)	C07D409-12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003031440	A1	WO 2002-US32628	20021011
US 2004034229	A1 Provisional	US 2001-329005P	20011012
		US 2002-269775	20021011
EP 1434775	A1	EP 2002-786395	20021011
		WO 2002-US32628	20021011
AU 2002351478	A1	AU 2002-351478	20021011
JP 2005505595	W	WO 2002-US32628	20021011
		JP 2003-534423	20021011
US 6903131	B2 Provisional	US 2001-329005P	20011012
		US 2002-269775	20021011
CN 1599734	A	CN 2002-824052	20021011
MX 2004003439	A1	WO 2002-US32628	20021011
		MX 2004-3439	20040412

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1434775	A1 Based on	WO 2003031440
AU 2002351478	A1 Based on	WO 2003031440
JP 2005505595	W Based on	WO 2003031440
MX 2004003439	A1 Based on	WO 2003031440

PRIORITY APPLN. INFO: US 2001-329005P 20011012; US
2002-269775 20021011

INT. PATENT CLASSIF.:

MAIN: A61K031-4015; C07D207-456; C07D409-12; C07D417-14
 SECONDARY: A61K031-337; A61K031-402; A61K031-4025; A61K031-4155;
 A61K031-4192; A61K031-4439; A61K031-454; A61K031-496;
 A61K031-506; A61K031-5377; A61K031-56; A61K038-00;
 A61K038-21; A61K038-22; A61K038-55; A61K039-395;
 A61K045-00; A61P001-02; A61P001-04; A61P001-16;
 A61P001-18; A61P003-10; A61P007-02; A61P009-00;
 A61P009-10; A61P009-12; A61P011-00; A61P011-06;
 A61P011-08; A61P011-10; A61P013-12; A61P017-02;
 A61P017-06; A61P019-02; A61P019-06; A61P019-10;
 A61P021-00; A61P025-00; A61P025-28; A61P027-02;
 A61P031-04; A61P031-18; A61P031-20; A61P031-22;
 A61P035-00; A61P037-06; A61P037-08; A61P043-00;
 C07D207-44; C07D401-08; C07D401-12; C07D403-12;
 C07D403-14; C07D405-12; C07D405-14; C07D409-14;
 C07D413-14; C07D417-12

BASIC ABSTRACT:

WO2003031440 A UPAB: 20030710

NOVELTY - 3,4-Disubstituted maleimide compounds (I) are new.

DETAILED DESCRIPTION - 3,4-Disubstituted maleimide compounds of formula (I), their salts or solvates are new.

U = e.g. aryl, heteroaryl, arylalkyl, heteroarylalkyl, cycloalkyl, heterocycloalkyl or cycloalkylalkyl (all optionally substituted);

A = e.g. pyridine, N-oxido-pyridine, furan, oxazole or imidazole (all optionally substituted), CR7R8-(CH₂)_n-CH=CR9 or a group of formula (i);

R7, R8 = e.g. H, alkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl;

R9 = e.g. halo, CF₃, 1H-tetrazol-5-yl or optionally substituted alkyl;

n = 0-6;

R8b = e.g. alkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl;

R9a = halo, CF₃ or CN;

m = 1-5;

n' = 0-4;

X = C, O, N or S; and

B = e.g. phenyl, 1H-benzotriazol-7-yl (all substituted).

Full Definitions are given in the DEFINITIONS (Full Definitions) field. INDEPENDENT CLAIMS are also included for:

(1) treatment of cancer or inhibition of angiogenesis involving administration of (I) and optionally at least one anti-cancer agent and/or radiation therapy; and

(2) inhibition of angiogenesis involving administration of (I) and optionally at least one anti-angiogenesis compound (A) or at least one anti-cancer agent and/or radiation therapy.

ACTIVITY - Antipsoriatic; Dermatological; Antiasthmatic; Respiratory; Antiarthritic; Antiinflammatory; Gastrointestinal; Antiulcer; Antibacterial; Immunosuppressive; Cerebroprotective; Cardiant; Nephrotropic; Thrombolytic; Nootropic; Neuroprotective; Protozoacide; Antiarteriosclerotic; Osteopathic; Vasotropic; Hepatotropic; Virucide; Anti-HIV; Cytostatic; Antitussive; Antipruritic; Tranquilizer; Vulnerary; Hemostatic; Ophthalmological; Antidiabetic; Antiseborrheic; Hypotensive; Antigout; Antialcoholic; Vulnerary.

MECHANISM OF ACTION - CXCR2 Receptor Binder; CXCR1 Receptor Binder; Angiogenesis Inhibitor; IL-8 Inhibitor.

Test details are described but no biological data is given.

USE - In the manufacture of a medicament for treating a chemokine-mediated disease e.g. psoriasis, atopic dermatitis, asthma, chronic obstructive pulmonary disease (COPD), adult respiratory disease, arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, septic shock, endotoxic shock, Gram negative sepsis, toxic shock syndrome, stroke, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, Alzheimer's disease, graft versus host reaction, allograft rejections, malaria, acute respiratory distress syndrome, delayed type hypersensitivity reaction, atherosclerosis, cerebral and cardiac ischemia, osteoarthritis, multiple sclerosis, restinosis, angiogenesis, osteoporosis, gingivitis, respiratory viruses, herpes viruses, hepatitis viruses, HIV, Kaposi's sarcoma associated virus, meningitis, cystic fibrosis, pre-term labor, cough, pruritis, multi-organ dysfunction, trauma, strains, sprains, contusions, psoriatic arthritis, herpes, encephalitis, CNS vasculitis, traumatic brain injury, CNS tumors, subarachnoid hemorrhage, post surgical trauma, interstitial pneumonitis, hypersensitivity, crystal induced arthritis, acute and chronic pancreatitis, acute alcoholic hepatitis, necrotizing enterocolitis, chronic sinusitis, angiogenic ocular disease, ocular inflammation, retinopathy of prematurity, diabetic retinopathy, macular degeneration with the wet type preferred and corneal neovascularization, polymyositis, vasculitis, acne, gastric and duodenal ulcers, celiac disease, esophagitis, glossitis, airflow obstruction, airway hyperresponsiveness, bronchiectasis, bronchiolitis, bronchiolitis obliterans, chronic bronchitis, cor pulmonae, cough, dyspnea, emphysema, hypercapnea, hyperinflation, hypoxemia, hyperoxia-induced inflammations, hypoxia, surgical lung volume reduction, pulmonary-fibrosis, pulmonary hypertension, right ventricular hypertrophy, peritonitis associated with

continuous ambulatory peritoneal dialysis (CAPD), granulocytic ehrlichiosis, sarcoidosis, small airway disease, ventilation-perfusion mismatching, wheeze, cold, gout, alcoholic liver disease, lupus, burn therapy, periodontitis, transplant reperfusion injury or early transplantation; and for treating cancer (all claimed).

Dwg.0/0

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: B01-D02; B02-T; B04-C01A; B04-G04; B04-G21;
B04-H02N; B04-H05A; B04-L04; B04-N04; B06-H; B07-H;
B10-A09B; B10-A18; B10-B01B; B14-A01; B14-A02;
B14-A03B; B14-C02; B14-C03; B14-C09; B14-E08;
B14-E10; B14-F01; B14-F02; B14-F04; B14-F05;
B14-F07; B14-F08; B14-G02A; B14-G02C; B14-H01;
B14-J01A4; B14-K01; B14-L06; B14-L07; B14-N01;
B14-N03; B14-N05; B14-N06; B14-N07A; B14-N10;
B14-N16; B14-N17A; B14-N17C; B14-S01; B14-S04;
B14-S06; D05-H11

TECH UPTX: 20030710

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) involves:

- (a) reacting a compound of formula (II) with SOCl_2 to form a compound of formula (III);
- (b) reacting (III) with BNH_2 to form a compound of formula (IV); and
- (c) reacting (IV) with ANH_2 .

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The anti-cancer agent is alkylating agent, antimetabolite, natural product and their derivative, hormone, anti-hormone, anti-angiogenic agent and steroid (including synthetic analog) or synthetics. (A) Is marimastat, AG3340, Col-3, Nevostat, BMS-275291, thalidomide, squalamine, endostatin, SU-5416, SU-6668, interferon-alpha, Anti-VEGF antibody, EMD-121974, CAI, interleukin-12, IM862, platelet factor-4, vitaxin, angiostatin, suramin, TNP-470, PTK-787, ZD-6474, ZD-101, Bay 129566, CGS27023A, VEGF receptor kinase inhibitor, taxotere or taxol.

L20 ANSWER 17 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-018873 [01] WPIX

DOC. NO. CPI: C2003-004640

TITLE: New 3,4-disubstituted cyclobutane-1,2-diones useful for the treatment of chemokine-mediated disease e.g. psoriasis.

DERWENT CLASS: B02 B05

INVENTOR(S): AKI, C J; BALDWIN, J J; BOND, R W; CHAO, J; DWYER, M; FERREIRA, J A; KAISER, B; LI, G; MERRITT, J R; NELSON, K H; PACTHER, J; ROKOSZ, L L; TAVERAS, A G; BALDWIN, H J; FERREIRA, J; TAVERAS, A; MERRITT, R J; PACTHER, J A

PATENT ASSIGNEE(S): (PHAR-N) PHARMACOPEIA INC; (SCHE) SCHERING CORP; (PHAR-N) PHARMACOPEIA DRUG DISCOVERY INC; (AKIC-I) AKI C J; (BALD-I) BALDWIN J J; (BOND-I) BOND R W; (CHAO-I) CHAO J; (DWYE-I) DWYER M; (FERR-I) FERREIRA J A; (KAIS-I) KAISER B; (LIGG-I) LI G; (MERR-I) MERRITT J R; (NELS-I) NELSON K H; (PACH-I) PACTHER J A; (ROKO-I) ROKOSZ L L; (TAVE-I) TAVERAS A G

COUNTRY COUNT: 98

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
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WO 2002076926 A1 20021003 (200301)* EN 113 C07C225-20
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM
 DZ EC EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT
 LU LV MA MD MG MK MN MX MZ NO NZ PH PL PT RO RU SE SG SI SK SL TJ
 TM TN TR TT TZ UA UZ VN YU ZA ZM
 US 2003097004 A1 20030522 (200336) C07D417-02
 US 2003204085 A1 20031030 (200372) C07D277-56
 NO 2003003424 A 20030930 (200373) C07C225-20
 EP 1355875 A1 20031029 (200379) EN C07C225-20
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 SK 2003000978 A3 20040108 (200413) C07C225-20
 BR 2002006968 A 20040309 (200420) C07C225-20
 KR 2003090629 A 20031128 (200420) C07C237-28
 CZ 2003002098 A3 20040114 (200429) A61P035-00
 AU 2002303084 A1 20021008 (200432) C07C225-20
 HU 2003004047 A2 20040428 (200435) C07C225-20
 JP 2004529911 W 20040930 (200465) 203 C07C221-00
 MX 2003006950 A1 20031201 (200470) A61K031-136
 US 2004235908 A1 20041125 (200478) A61K031-44
 ZA 2003005881 A 20050126 (200513) 123 C07C000-00
 CN 1575273 A 20050202 (200532) C07C225-20
 IN 2003001171 P4 20050422 (200560) EN C07C225-20
 NZ 527947 A 20051028 (200581) C07C225-20

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002076926	A1	WO 2002-US2888	20020201
US 2003097004	A1 Provisional	US 2001-265951P	20010202
		US 2002-62006	20020201
US 2003204085	A1 Provisional	US 2001-265951P	20010202
	CIP of	US 2002-62006	20020201
		US 2002-208426	20020730
NO 2003003424	A	WO 2002-US2888	20020201
		NO 2003-3424	20030731
EP 1355875	A1	EP 2002-731085	20020201
		WO 2002-US2888	20020201
SK 2003000978	A3	WO 2002-US2888	20020201
		SK 2003-978	20020201
BR 2002006968	A	BR 2002-6968	20020201
		WO 2002-US2888	20020201
KR 2003090629	A	KR 2003-709958	20030728
CZ 2003002098	A3	WO 2002-US2888	20020201
		CZ 2003-2098	20020201
AU 2002303084	A1	AU 2002-303084	20020201
HU 2003004047	A2	WO 2002-US2888	20020201
		HU 2003-4047	20020201
JP 2004529911	W	JP 2002-576189	20020201
		WO 2002-US2888	20020201
MX 2003006950	A1	WO 2002-US2888	20020201
		MX 2003-6950	20030801
US 2004235908	A1 Provisional	US 2001-265951P	20010202
	CIP of	US 2002-62006	20020201
	Div ex	US 2002-208426	20020730
		US 2004-869189	20040616
ZA 2003005881	A	ZA 2003-5881	20030730

CN 1575273	A	CN 2002-804517	20020201
IN 2003001171	P4	IN 2003-CN1171	20030729
		WO 2002-US2888	
NZ 527947	A	NZ 2002-527947	20020201
		WO 2002-US2888	20020201

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1355875	A1 Based on	WO 2002076926
SK 2003000978	A3 Based on	WO 2002076926
BR 2002006968	A Based on	WO 2002076926
CZ 2003002098	A3 Based on	WO 2002076926
AU 2002303084	A1 Based on	WO 2002076926
HU 2003004047	A2 Based on	WO 2002076926
JP 2004529911	W Based on	WO 2002076926
MX 2003006950	A1 Based on	WO 2002076926
NZ 527947	A Based on	WO 2002076926

PRIORITY APPLN. INFO: US 2001-265951P 20010202; US
 2002-62006 20020201; US
 2002-208426 20020730; US
 2004-869189 20040616

INT. PATENT CLASSIF.:

MAIN:

A61K031-136; A61K031-44; A61P035-00; C07C000-00;
 C07C221-00; C07C225-20; C07C237-28; C07D277-56;
 C07D417-02

SECONDARY:

A61K031-166; A61K031-167; A61K031-18; A61K031-192;
 A61K031-198; A61K031-216; A61K031-24; A61K031-27;
 A61K031-277; A61K031-36; A61K031-397; A61K031-40;
 A61K031-415; A61K031-4174; A61K031-4184; A61K031-4192;
 A61K031-426; A61K031-433; A61K031-4402; A61K031-4406;
 A61K031-445; A61K031-4453; A61K031-495; A61K031-505;
 A61K031-5375; A61P001-00; A61P007-00; A61P007-02;
 A61P009-10; A61P011-00; A61P011-06; A61P013-12;
 A61P017-00; A61P017-06; A61P019-02; A61P025-08;
 A61P025-28; A61P027-02; A61P029-00; A61P031-04;
 A61P031-18; A61P031-22; A61P033-06; A61P037-02;
 A61P037-08; A61P043-00; C07C225-18; C07C229-42;
 C07C229-64; C07C237-36; C07C237-44; C07C255-58;
 C07C255-59; C07C271-20; C07C311-08; C07C311-21;
 C07D205-04; C07D207-08; C07D207-16; C07D211-60;
 C07D213-89; C07D231-38; C07D235-06; C07D239-42;
 C07D249-18; C07D257-04; C07D263-34; C07D277-28;
 C07D285-08; C07D295-13; C07D295-135; C07D295-192;
 C07D295-205; C07D317-66; C07D333-38; C07D405-12;
 C07D413-02; C07D521-00

BASIC ABSTRACT:

WO 200276926 A UPAB: 20030101

NOVELTY - New 3,4-Disubstituted cyclobutane-1,2-diones.

DETAILED DESCRIPTION - 3,4-Disubstituted cyclobutane-1,2-diones of formula (I), their prodrugs, salts, solvates or isomers are new.

A = optionally substituted (hetero)aryl;

B = phenyl (substituted at 2 - 6-position by R2 - R6 respectively), benzotriazole-7-yl (substituted at 4 - 6-position by R4 - R6 respectively), benzoimidazole-7-yl (substituted at 2 - 6-position by R9 and R4 - R6 respectively), indole-7-yl (substituted at 2 - 6-position by R9, R10 and R4 - R6 respectively), indazole-7-yl (substituted at 3 - 6-position by R10 and R4 - R6 respectively), pyrazol-4-ol-3-yl (substituted

at 1 and 5- position by R15 and R3), thiophene-3-ol-4-yl (substituted at 3- and 5- position by R3 and R15), pyrazol-4-ol-5-yl (substituted at 1- and 3- position by R3 and R15), pyrrol-3-ol-4-yl (substituted at 1-, 1- and 5- position by R15, R9 and 2-position by R3), or pyrrol-3-ol-2-yl (substituted at 1-, 4- and 5- position by R15, R3 and R9 respectively);

R2 = H, OH, C(O)OH, SH, SO₂NR₇R₈, NHC(O)R₇, NHSO₂NR₇R₈, NHSO₂R₇, C(O)NR₇R₈, C(O)NR₇OR₈, OR₁₃ or optionally substituted heterocyclic acidic functional group;

R3 and R4 = alkyl, (hetero)aryl (both optionally substituted), T, OH, SOR₇, or R₈-C(=N)-OR₇;

T = H, halo, alkoxy, CF₃, OCF₃, NO₂, C(O)R₇, C(O)OR₇, C(O)NR₇R₈, SOR₇NR₇R₈, C(O)NR₇OR₈ or cyano;

R5 and R6 = optionally substituted (hetero)aryl, T or alkyl;

R7 and R8 = alkyl, (hetero)aryl, (hetero)alkylaryl, (hetero)arylalkyl or cycloalkyl (all optionally substituted), H, carboxyalkyl or aminoalkyl;

NR₇R₈+NR₇OR₈ = 3 - 7 membered ring containing 1 - 3 heteroatoms (optionally substituted by at least one OH, cyano, carboxyl, hydroxyalkyl, alkoxy, COR₇R₈ or aminoalkyl);

R9 and R10 = H, halo, CF₃, OCF₃, NR₇R₈, NR₇C(O)NR₇R₈, OH, C(O)OR₇, SH, SOR₇NR₇R₈, SO₂R₇, NHC(O)R₇, NHSO₂NR₇R₈, NHSO₂R₇, C(O)NR₇R₈, C(O)NR₇OR₈, OR₁₃ or optionally substituted heterocyclic acidic functional group;

R13 = COR₇;

R15 = (hetero)aryl, arylalkyl, cycloalkyl, alkyl (all optionally substituted), H or OR₁₃;

t = 1 or 2.

INDEPENDENT CLAIMS are included for the following:

(1) Inhibition of angiogenesis involving administering (I); and

(2) Treatment of cancer involving administering (I).

ACTIVITY - Antipsoriatic; Antiasthmatic; Antiarthritic; Antiinflammatory; Antiulcer; Antibacterial; Immunosuppressive; Cerebroprotective; Cardiant; Vasotropic; Nephrotropic; Thrombolytic; Nootropic; Neuroprotective; Protozoacide; Antiarteriosclerotic; Cytostatic; Anti-HIV; Antidiabetic; Dermatological.

MECHANISM OF ACTION - CXC-chemokine (preferably CXCR2 and CXCR1) receptor binder; Interleukin-8 (IL-8) receptor binder; Vascular endothelial growth factor (VEGF) receptor kinase inhibitor; GRO-alpha chemokine inhibitor.

Test details are described. (I) showed % inhibition of 250 nM for CXCR1 SPA assay. No results for specific compounds are given.

USE - For the treatment of chemokine-mediated disease (e.g. psoriasis, atopic dermatitis, asthma, chronic obstructive pulmonary disease, adult respiratory disease, arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, stroke, cardiac and renal reperfusion injury, glomerulonephritis or thrombosis, Alzheimer's disease, graft vs. host reaction, allograft rejections, malaria, acute respiratory distress syndrome, delayed type hypersensitivity reaction, atherosclerosis, cerebral and cardiac ischemia); for the treatment of cancer (e.g. melanoma, gastric carcinoma or non-small lung carcinoma), gingivitis, respiratory viruses, herpes viruses, hepatitis viruses, HIV, kaposi's sarcoma associated virus, angiogenesis including angiogenic ocular disease (e.g. ocular inflammation, retinopathy of prematurity, diabetic retinopathy, macular degeneration, corneal neovascularization) (all claimed).

ADVANTAGE - (I) exhibits CXC-chemokine receptor and IL-8 receptor binding modulatory activity.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: B10-B01A; B14-A02A5; B14-A02A7; B14-A02A8;
 B14-A02B1; B14-A02B3; B14-A03B; B14-C09; B14-D06;
 B14-E10C; B14-F01; B14-F02F2; B14-F04; B14-F07;
 B14-G02C; B14-H01; B14-J01; B14-J01A4; B14-K01;
 B14-K01F; B14-N03; B14-N06B; B14-N16; B14-N17C;
 B14-S06

TECH UPTX: 20030101

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) (where B is phenyl substituted by -C(O)-NR7R8) involves:

(1) Condensation of an amine of formula NR7R8H with a nitrosalicylic acid under coupling conditions and resulting nitrobenzamide is reduced under H2 atmosphere in the presence of a catalyst to form compound of formula (Ib);
 (2) Condensing an aryl amine of formula A-NH2 with diethylsquarate to give anilinoethoxysquarate of formula (Ic); and condensation of (Ic) with (Ib).
 Preferred Method: Inhibition of angiogenesis further involves administering at least one anti-angiogenic agent. Treatment of cancer further involves administering at least one anticancer agent and/or radiation therapy.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Agents: The anti-cancer agent is alkylating agents, antimetabolites, natural products, hormones, anti-hormones, anti-angiogenic agents, steroids or synthetics. The anti-angiogenic agent is Marimastat, AG3340, Col-3, Neovastat, BMS-275291, Thalidomide, Squalamine, Endostatin, SU-5416, SU-6668, Interferon-alpha, Anti-VEGF antibody, EMD121974, CAI, Interleukin-12, IM862, Platelet Factor-4, Vitaxin, Angiostatin, Suramin, TNP-470, PTK-787, ZD-6474, ZD-101, Bay 129566, CGS27023A, VEGF receptor kinase inhibitor, taxotere or Taxol.

L20 ANSWER 18 OF 18 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 1999-080943 [07] WPIX
 DOC. NO. CPI: C1999-024313
 TITLE: New benzo-cyclohepta-pyridine derivatives - used as farnesyl protein transferase inhibitors and antitumour agents, e.g. for treating lung cancer or myeloid leukaemia.
 DERWENT CLASS: B02
 INVENTOR(S): GUZI, T J; RANE, D F
 PATENT ASSIGNEE(S): (SCHE) SCHERING CORP
 COUNTRY COUNT: 80
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 9857945	A1	19981223	(199907)*	EN	76	C07D401-04	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL							
OA PT SD SE SZ UG ZW							
W: AL AM AU AZ BA BB BG BR BY CA CN CZ EE GE GW HU ID IL IS JP KG KR							
KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM							
TR TT UA UZ VN YU							
AU 9879537	A	19990104	(199921)			C07D401-04	
EP 991637	A1	20000412	(200023)	EN		C07D401-04	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE							
CN 1272844	A	20001108	(200114)			C07D401-04	
MX 9912077	A1	20000801	(200137)			C07D401-04	
HU 2000002659	A2	20010628	(200143)			C07D401-04	
KR 2001013829	A	20010226	(200154)			C07D401-04	
JP 2002510308	W	20020402	(200225)		88	C07D401-04	
EP 991637	B1	20020529	(200236)	EN		C07D401-04	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE							

DE 69805619	E	20020704 (200251)	C07D401-04
ES 2174450	T3	20021101 (200279)	C07D401-04
MX 215282	B	20030716 (200462)	A61K031-435

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9857945	A1	WO 1998-US11499	19980615
AU 9879537	A	AU 1998-79537	19980615
EP 991637	A1	EP 1998-930063	19980615
		WO 1998-US11499	19980615
CN 1272844	A	CN 1998-808206	19980615
MX 9912077	A1	MX 1999-12077	19991217
HU 2000002659	A2	WO 1998-US11499	19980615
		HU 2000-2659	19980615
KR 2001013829	A	KR 1999-711849	19991215
JP 2002510308	W	WO 1998-US11499	19980615
		JP 1999-504494	19980615
EP 991637	B1	EP 1998-930063	19980615
		WO 1998-US11499	19980615
DE 69805619	E	DE 1998-605619	19980615
		EP 1998-930063	19980615
		WO 1998-US11499	19980615
ES 2174450	T3	EP 1998-930063	19980615
MX 215282	B	WO 1998-US11499	19980615
		MX 1999-12077	19991217

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9879537	A Based on	WO 9857945
EP 991637	A1 Based on	WO 9857945
HU 2000002659	A2 Based on	WO 9857945
JP 2002510308	W Based on	WO 9857945
EP 991637	B1 Based on	WO 9857945
DE 69805619	E Based on	EP 991637
	Based on	WO 9857945
ES 2174450	T3 Based on	EP 991637
MX 215282	B Based on	WO 9857945

PRIORITY APPLN. INFO: US 1997-876507 19970617

INT. PATENT CLASSIF.:

MAIN: A61K031-435; C07D401-04
 SECONDARY: A61K031-4545; A61K031-496; A61K031-497; A61K031-5377;
 A61P035-00; A61P043-00; C07D221-16; C07D401-12;
 C07D401-14

BASIC ABSTRACT:

WO 9857945 A UPAB: 19990217
 Benzo (5,6) cyclohepta (1,2-b) pyridine derivatives of formula (I) and their salts and solvates are new. a = 0 or 1; R1, R3 = halo; R2, R4 = H or halo, provided that at least one is H; dotted line = optional bond; X = N, C or CH; T = -(CHR5)b-Y-(CHR5)c-C(O)Z; R5 = H, 1-6C alkyl or bond; b,c = 0-3; Y = cyclopropane-1,2-diyl, cyclobutanediyl, cyclopentanediy, phenylene, pyridinediyl or pyrazinediyl, all substituted by two R6 groups; or cyclohexanediy, substituted by three R6 groups; R6 = H or 1-6C alkyl; Z = OR7, R7 or NR8R9; R7 = H or 1-6C alkyl (optionally substituted by OR5, COR5, phenyl or heteroaryl); R8, R9 = H, OH or 1-6C alkyl (optionally substituted by OR5, COR5, phenyl or heteroaryl); or

NR8R9 = 5- or 6-membered heterocyclic ring system containing 1-4 of N, O, S, SO and SO₂, optionally substituted by 1-8C alkanoyl, 1-6C alkyl or 1-6C perhaloalkyl.

USE - (I) are farnesyl protein transferase (FTP) inhibitors (claimed), and are used to inhibit or treat the abnormal growth of cells in mammals, especially humans. (I) are especially used to treat tumour cells expressing an active ras oncogene, specifically pancreatic, lung, myeloid leukaemia, thyroid follicular, myelodysplastic, epidermal or bladder carcinoma, colon, breast or prostate tumour cells (all claimed). (I) may also be used to treat tumour cells in which the Ras protein is activated as a result of oncogenic mutation in genes other than the ras gene (claimed), e.g. to inhibit or treat proliferative diseases (benign and malignant) in which Ras proteins are activated aberrantly as a result of oncogenic mutations in other genes, such as neurofibromatosis or tumours in which Ras is activated due to mutation or over-expression of tyrosine kinase oncogenes.

ADVANTAGE - (I) potentially inhibit FTP, but not geranylgeranyl protein transferase I in vitro; block the phenotypic change induced by a form of transforming Ras that is a farnesyl acceptor but not by a form of transforming Ras engineered to be a geranylgeranyl acceptor; block intracellular processing of Ras, which is a farnesyl acceptor, but not of Ras engineered to be a geranylgeranyl acceptor; and block abnormal cell growth in culture induced by transforming Ras.

Dwg.0/0

FILE SEGMENT:	CPI
FIELD AVAILABILITY:	AB; GI; DCN
MANUAL CODES:	CPI: B06-D13; B14-D06; B14-H01

=>

=> => fil reg; d stat que l31

FILE 'REGISTRY' ENTERED AT 12:05:25 ON 19 JUN 2006

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STRUCTURE FILE UPDATES: 16 JUN 2006 HIGHEST RN 888069-20-3

DICTIONARY FILE UPDATES: 16 JUN 2006 HIGHEST RN 888069-20-3

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

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*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
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Structure search iteration limits have been increased. See HELP SLIMITS
for details.

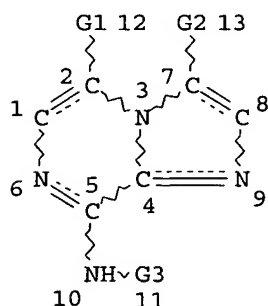
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d stat que l29; d que nos l33

L21

STR



Ak @14

CH~G4~Hy
@15 16 17

C≡O
@18 19

*full file search done
on this structure*

VAR G1=H/X/14

VAR G2=H/X/CY/14/CF3

VAR G3=CB/15/SO2/18

REP G4=(0-3) CH

NODE ATTRIBUTES:

CONNECT IS E1 C AT 1
CONNECT IS E1 RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L29 474 SEA FILE=REGISTRY SSS FUL L21

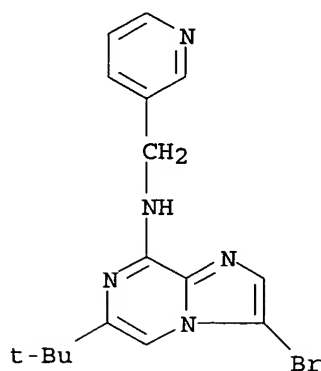
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SEARCH TIME: 00.00.01

474 ANSWERS

L21 STR
L29 474 SEA FILE=REGISTRY SSS FUL L21
L30 200 SEA FILE=REGISTRY ABB=ON C16H18BRN5?/MF
L31 2 SEA FILE=REGISTRY ABB=ON L30 AND L29
L33 1 SEA FILE=REGISTRY ABB=ON L31 AND 3-BROMO

=> d ide l33

L33 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 676132-56-2 REGISTRY
ED Entered STN: 19 Apr 2004
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(1,1-dimethylethyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C16 H18 Br N5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil capl uspatf toxcenter; s l33
 FILE 'CAPLUS' ENTERED AT 12:06:33 ON 19 JUN 2006
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 CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 12:06:33 ON 19 JUN 2006
 COPYRIGHT (C) 2006 ACS

L34 3 L33

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 PROCESSING COMPLETED FOR L34
 L35 2 DUP REM L34 (1 DUPLICATE REMOVED)
 ANSWER '1' FROM FILE CAPLUS
 ANSWER '2' FROM FILE USPATFULL

=> d ibib ed abs hitrn 1-2

L35 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2004:267246 CAPLUS
 DOCUMENT NUMBER: 140:303696
 TITLE: Preparation and pharmaceutical compositions of novel
 imidazopyrazines as cyclin dependent kinase inhibitors
 INVENTOR(S): Paruch, Kamil; Guzi, Timothy J.; Dwyer, Michael P.;
 Doll, Ronald J.; Girijavallabhan, Viyyoor M.
 PATENT ASSIGNEE(S): Schering Corporation, USA
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026310	A1	20040401	WO 2003-US29456	20030919
WO 2004026310	C1	20050630		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2499874	AA	20040401	CA 2003-2499874	20030919
AU 2003275031	A1	20040408	AU 2003-275031	20030919
US 2004072835	A1	20040415	US 2003-666424	20030919
EP 1542693	A1	20050622	EP 2003-759300	20030919
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006503838	T2	20060202	JP 2004-538213	20030919
ZA 2005002380	A	20050927	ZA 2005-2380	20050322

PRIORITY APPLN. INFO.:

US 2002-412906P

P 20020923

WO 2003-US29456

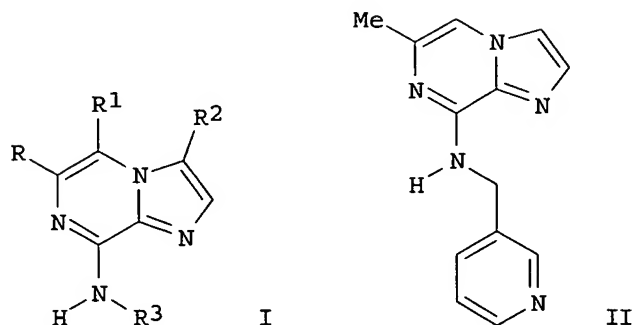
W 20030919

OTHER SOURCE(S):

MARPAT 140:303696

ED Entered STN: 01 Apr 2004

GI



AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compds. I [R = CF₃, (un)substituted-alkyl, -heteroaryl, -heteroarylalkyl, -cycloalkyl, -heterocyclyl, etc.; R¹ = H, halo or alkyl; R² = H, halo, CN, cycloalkyl, heterocyclyl, alkynyl and CF₃; R³ = aryl (with exception of Ph), (un)substituted-heteroaryl (with exception of furyl), -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by substitution of 8-chloro-6-methylimidzol[1,2-a]pyrazine with 3-(aminomethyl)pyridine. Methods for performing assays with I are described (no data).

IT 676132-56-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 2 OF 2 USPATFULL on STN

ACCESSION NUMBER: 2004:95380 USPATFULL

TITLE: Novel imidazopyrazines as cyclin dependent kinase inhibitors

INVENTOR(S): Paruch, Kamil, Garwood, NJ, UNITED STATES
Guzi, Timothy J., Chatham, NJ, UNITED STATES
Dwyer, Michael P., Scotch Plains, NJ, UNITED STATES
Doll, Ronald J., Convent Station, NJ, UNITED STATES
Girijavallabhan, Viyyoor M., Parsippany, NJ, UNITED STATES

PATENT ASSIGNEE(S): SCHERING CORPORATION (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004072835	A1	20040415

APPLICATION INFO.: US 2003-666424 A1 20030919 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-412906P	20020923 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530	
NUMBER OF CLAIMS:	27	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1213	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compounds as inhibitors of cyclin dependent kinases, methods of preparing such compounds, pharmaceutical compositions containing one or more such compounds, methods of preparing pharmaceutical formulations comprising one or more such compounds, and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compounds or pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 676132-56-2P

(drug candidate; preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors)

=>

=> => fil reg; d stat que 129; fil capl; d que nos 136
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STRUCTURE FILE UPDATES: 18 JUN 2006 HIGHEST RN 888212-64-4
 DICTIONARY FILE UPDATES: 18 JUN 2006 HIGHEST RN 888212-64-4

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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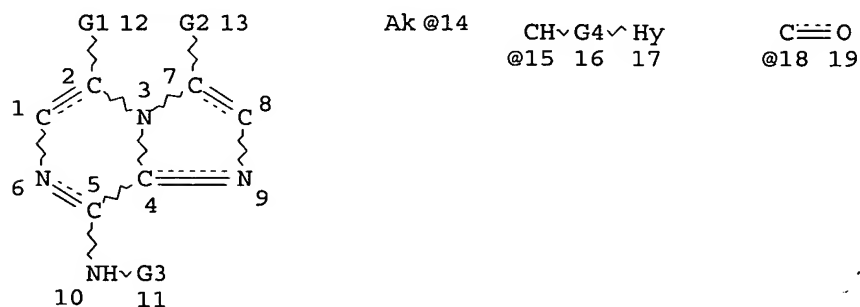
 *
 * type information have been removed from *
 * default display format and the ED field has been added, *
 * effective March 20, 2005. A new display format, IDERL, is now *
 * available and contains the CA role and document type information. *
 *

Structure search iteration limits have been increased. See HELP SLIMITS
 for details.

REGISTRY includes numerically searchable data for experimental and
 predicted properties as well as tags indicating availability of
 experimental property data in the original document. For information
 on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

L21 STR



VAR G1=H/X/14
 VAR G2=H/X/CY/14/CF3
 VAR G3=CB/15/SO2/18
 REP G4=(0-3) CH
 NODE ATTRIBUTES:

CONNECT IS E1 C AT 1
CONNECT IS E1 RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L29 474 SEA FILE=REGISTRY SSS FUL L21

100.0% PROCESSED 10269 ITERATIONS 474 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 12:08:24 ON 19 JUN 2006
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FILE COVERS 1907 - 19 Jun 2006 VOL 144 ISS 26
FILE LAST UPDATED: 18 Jun 2006 (20060618/ED)

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<http://www.cas.org/infopolicy.html>
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L21 STR
L29 474 SEA FILE=REGISTRY SSS FUL L21
L36 16 SEA FILE=CAPLUS ABB=ON L29

=> s l36 not l33

1 L33

L38

15 L36 NOT L33

previously printed

=> d ibib ed abs hitstr l38 1-15; fil hom

L38 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:463553 CAPLUS
DOCUMENT NUMBER: 144:488677
TITLE: Preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.;
Zhao, Lianyun; Curran, Patrick J.; Belanger, David B.;
Hamann, Blake; Reddy, Panduranga A.; Siddiqui, M.
Arshad

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 161 pp., Cont.-in-part of U.S.
Ser. No. 47,524.
CODEN: USXXCO

DOCUMENT TYPE: Patent

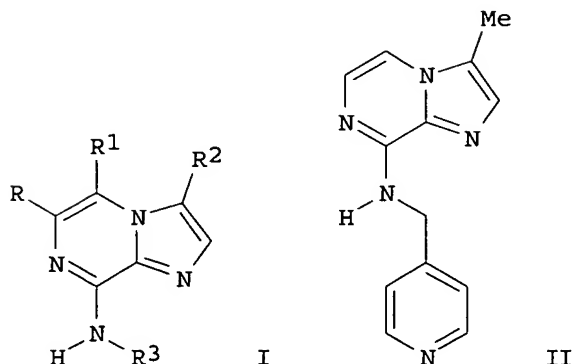
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006106023	A1	20060518	US 2005-272392	20051110
US 2004063715	A1	20040401	US 2003-665005	20030919
US 6919341	B2	20050719		
US 2005130980	A1	20050616	US 2005-47524	20050131
PRIORITY APPLN. INFO.:			US 2002-412997P	P 20020923
			US 2003-665005	A3 20030919
			US 2005-47524	A2 20050131

ED Entered STN: 18 May 2006
GI



AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-*a*]pyrazine compds. of formula I [R = H, halo, (un)substituted-aryl, -heteroaryl, -cycloalkyl, etc.; R1 = H, halo or alkyl; R2 = halo, (un)substituted-alkyl, -aryl, -arylalkyl, etc.; R3 = H, (un)substituted-aryl, -heteroaryl, -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by condensation of 8-chloro-3-methylimidazo[1,2-*a*]pyrazine with 4-(aminomethyl)pyridine. I possessed excellent CDK inhibitory properties, e.g., II demonstrated an IC50 value of 22.5 μ M.

IT 676359-74-3P 676359-80-1P 676359-82-3P
676359-86-7P 676360-15-9P 676360-29-5P

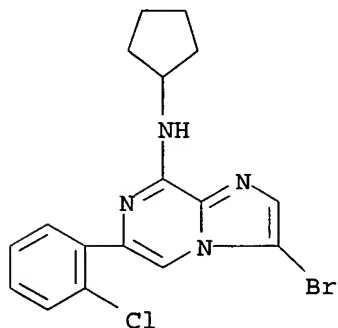
676360-33-1P 676360-35-3P 676360-37-5P
676360-39-7P 676360-41-1P 676360-43-3P
676360-49-9P 676360-51-3P 676360-53-5P
676360-55-7P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU
(Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study);
PREP (Preparation); USES (Uses)

(drug candidate; preparation of novel imidazopyrazines as cyclin dependent
kinase inhibitors useful in treatment and prevention of various
diseases)

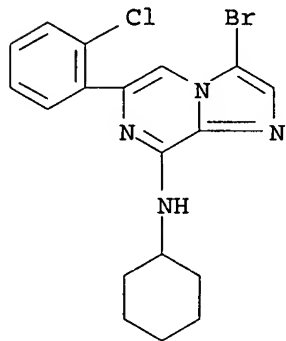
RN 676359-74-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-cyclopentyl-
(9CI) (CA INDEX NAME)



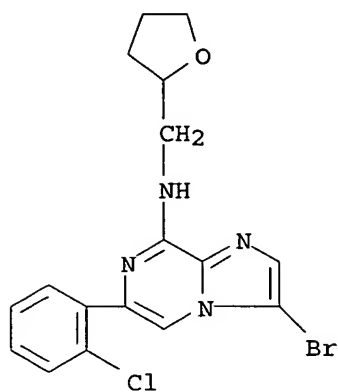
RN 676359-80-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-cyclohexyl-
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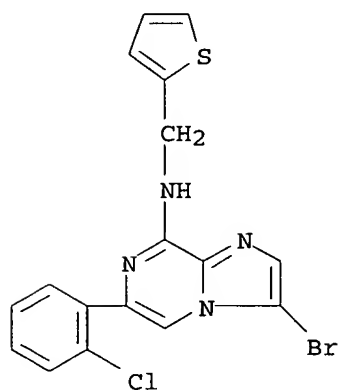
RN 676359-82-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[(tetrahydro-2-
furanyl)methyl]- (9CI) (CA INDEX NAME)



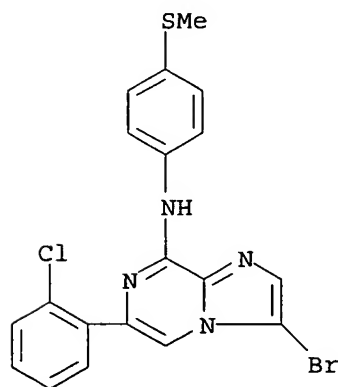
RN 676359-86-7 CAPLUS

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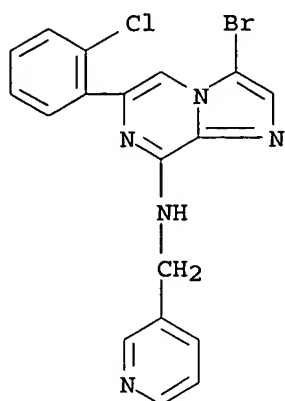
RN 676360-15-9 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[4-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



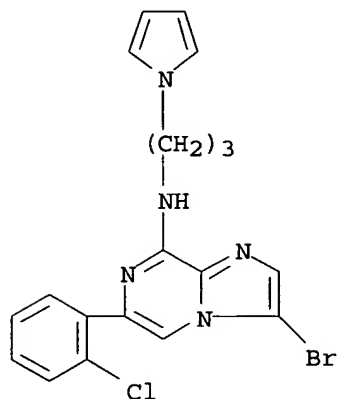
RN 676360-29-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



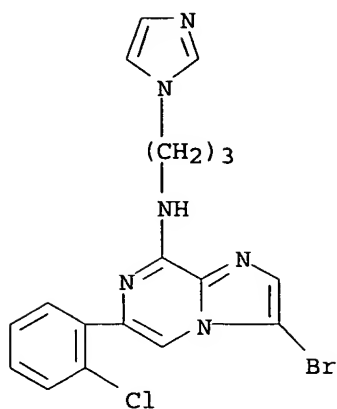
RN 676360-33-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1H-pyrrol-1-yl)propyl]- (9CI) (CA INDEX NAME)



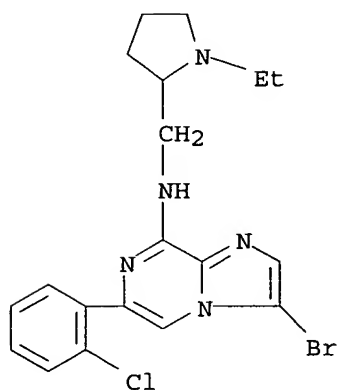
RN 676360-35-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



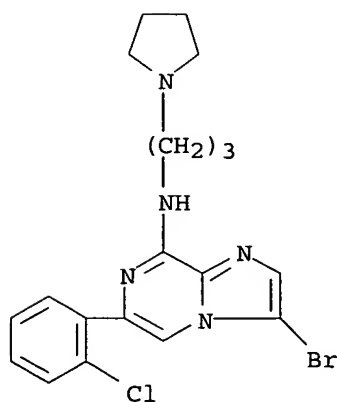
RN 676360-37-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[(1-ethyl-2-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



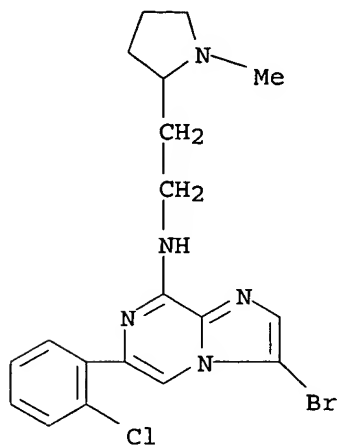
RN 676360-39-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)



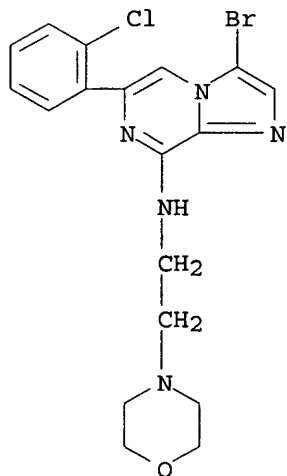
RN 676360-41-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



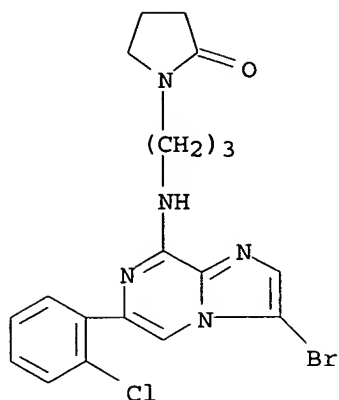
RN 676360-43-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



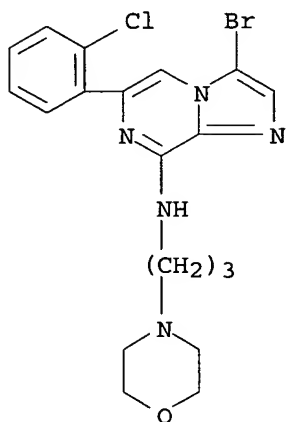
RN 676360-49-9 CAPLUS

CN 2-Pyrrolidinone, 1-[3-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]propyl]- (9CI) (CA INDEX NAME)



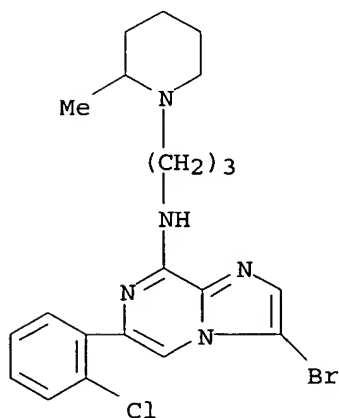
RN 676360-51-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

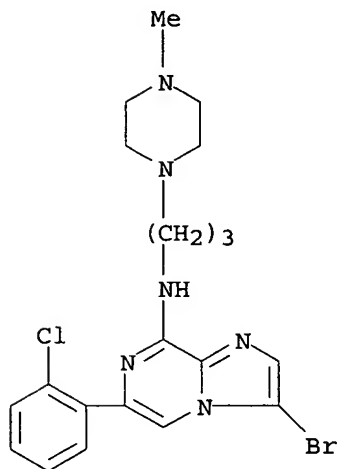


RN 676360-53-5 CAPLUS

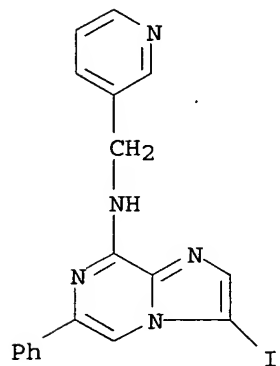
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(2-methyl-1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



RN 676360-55-7 CAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



IT 676360-96-6P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (drug candidate; preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors useful in treatment and prevention of various diseases)
 RN 676360-96-6 CAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-iodo-6-phenyl-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



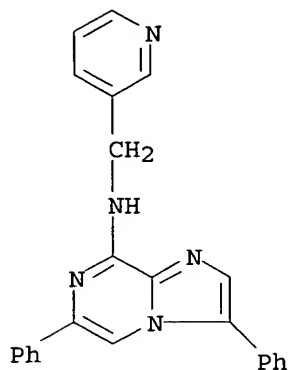
IT 676359-47-0P 676359-49-2P 676359-51-6P
 676359-70-9P 676360-59-1P 676360-61-5P
 676360-63-7P 676360-65-9P 676360-67-1P
 676360-69-3P 676360-71-7P 676360-73-9P
 676360-76-2P 676360-78-4P 676360-80-8P
 676360-82-0P 676360-84-2P 676360-86-4P
 676360-89-7P 676360-91-1P 676360-94-4P
 676360-98-8P 676361-00-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(drug candidate; preparation of novel imidazopyrazines as cyclin dependent
kinase inhibitors useful in treatment and prevention of various
diseases)

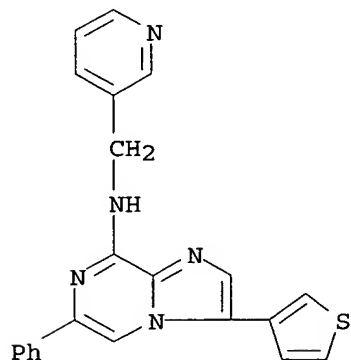
RN 676359-47-0 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3,6-diphenyl-N-(3-pyridinylmethyl)- (9CI)
(CA INDEX NAME)



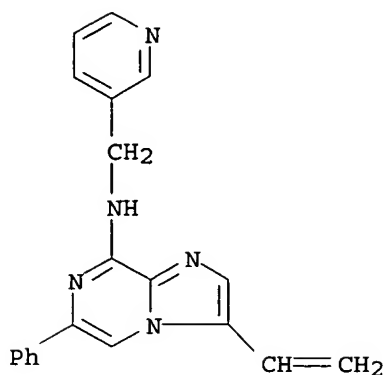
RN 676359-49-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl-N-(3-pyridinylmethyl)-3-(3-thienyl)- (9CI) (CA INDEX NAME)

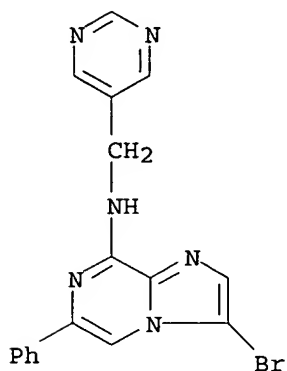


RN 676359-51-6 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-ethenyl-6-phenyl-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

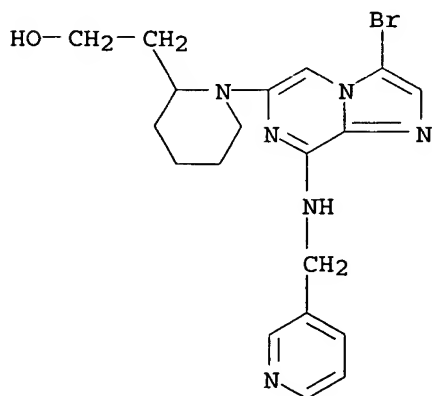


RN 676359-70-9 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(5-pyrimidinylmethyl)-
(9CI) (CA INDEX NAME)

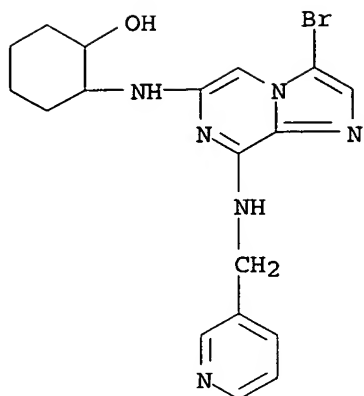
RN 676360-59-1 CAPLUS

CN 2-Piperidineethanol, 1-[3-bromo-8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



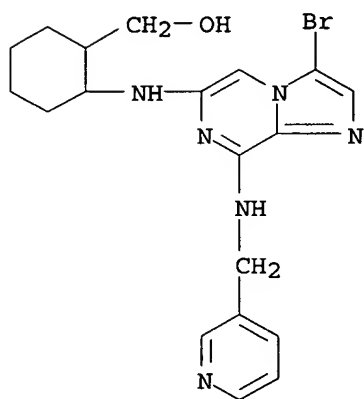
RN 676360-61-5 CAPLUS

CN Cyclohexanol, 2-[[[3-bromo-8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]amino]- (9CI) (CA INDEX NAME)



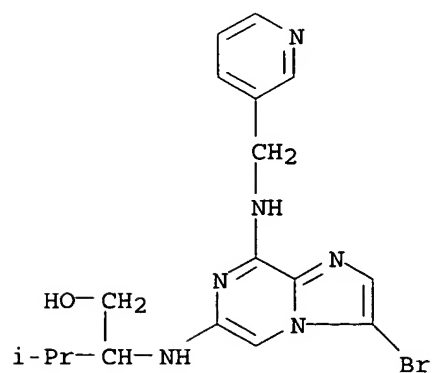
RN 676360-63-7 CAPLUS

CN Cyclohexanemethanol, 2-[[3-bromo-8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]amino]- (9CI) (CA INDEX NAME)



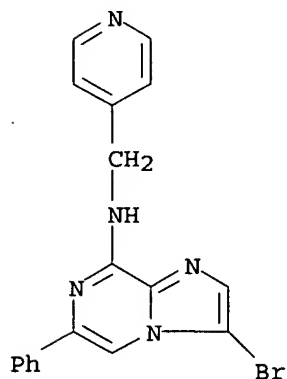
RN 676360-65-9 CAPLUS

CN 1-Butanol, 2-[[3-bromo-8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]amino]-3-methyl- (9CI) (CA INDEX NAME)

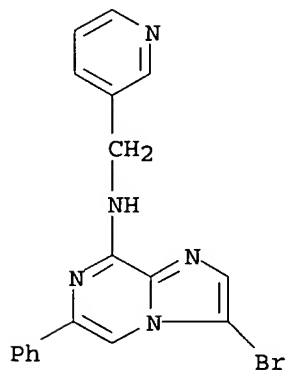


RN 676360-67-1 CAPLUS

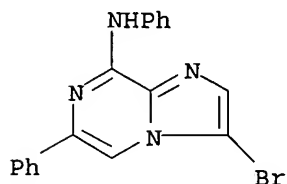
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(4-pyridinylmethyl)-
(9CI) (CA INDEX NAME)



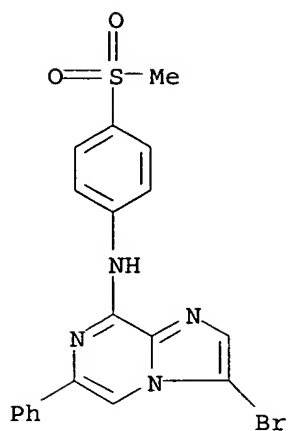
RN 676360-69-3 CAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(3-pyridinylmethyl)-
(9CI) (CA INDEX NAME)



RN 676360-71-7 CAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N,6-diphenyl- (9CI) (CA INDEX
NAME)

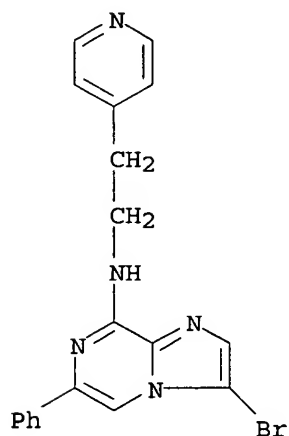


RN 676360-73-9 CAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N-[4-(methylsulfonyl)phenyl]-6-
phenyl- (9CI) (CA INDEX NAME)



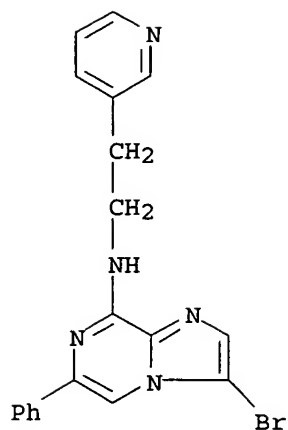
RN 676360-76-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[2-(4-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)



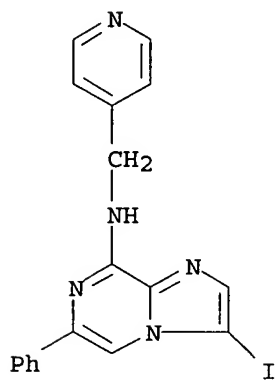
RN 676360-78-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[2-(3-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)



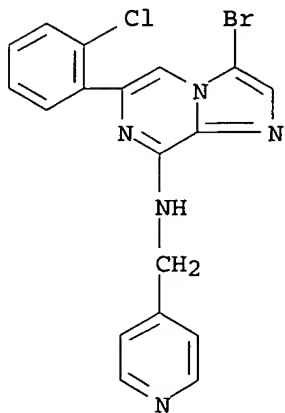
RN 676360-80-8 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-iodo-6-phenyl-N-(4-pyridinylmethyl) - (9CI) (CA INDEX NAME)



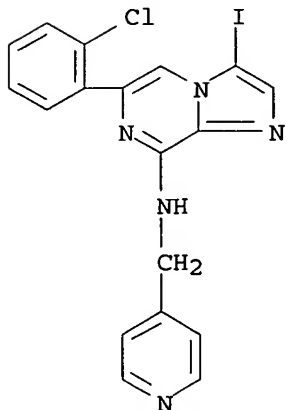
RN 676360-82-0 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(4-pyridinylmethyl) - (9CI) (CA INDEX NAME)



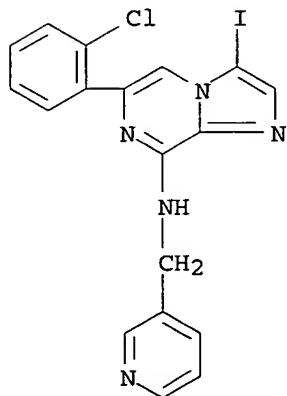
RN 676360-84-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-3-iodo-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



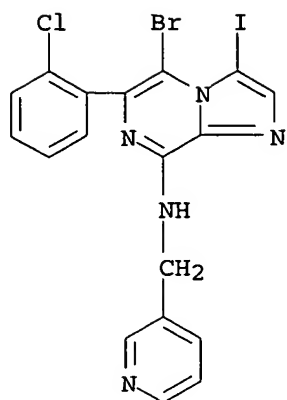
RN 676360-86-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-3-iodo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



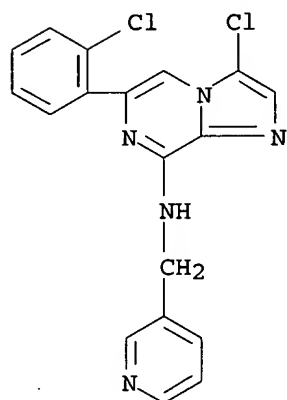
RN 676360-89-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 5-bromo-6-(2-chlorophenyl)-3-iodo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



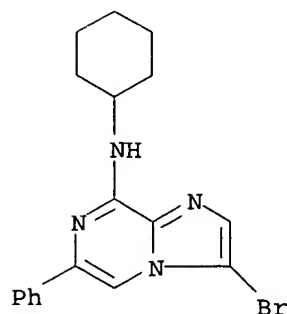
RN 676360-91-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-chloro-6-(2-chlorophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



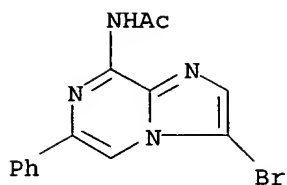
RN 676360-94-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N-cyclohexyl-6-phenyl- (9CI) (CA INDEX NAME)



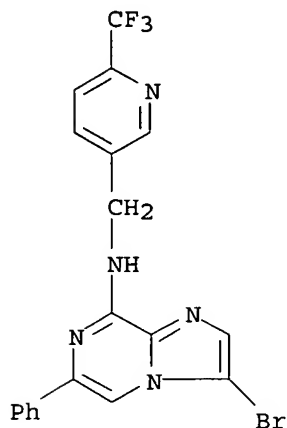
RN 676360-98-8 CAPLUS

CN Acetamide, N-(3-bromo-6-phenylimidazo[1,2-a]pyrazin-8-yl)- (9CI) (CA INDEX NAME)



RN 676361-00-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[[6-(trifluoromethyl)-3-pyridinyl]methyl]- (9CI) (CA INDEX NAME)



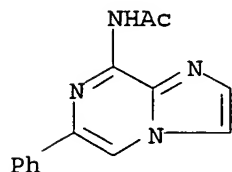
IT 676361-14-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors useful in treatment and prevention of various diseases)

RN 676361-14-1 CAPLUS

CN Acetamide, N-(6-phenylimidazo[1,2-a]pyrazin-8-yl)- (9CI) (CA INDEX NAME)



IT 887475-23-2P 887475-26-5P 887475-29-8P

887475-30-1P 887475-31-2P 887475-34-5P

887475-37-8P 887475-38-9P 887476-02-0P

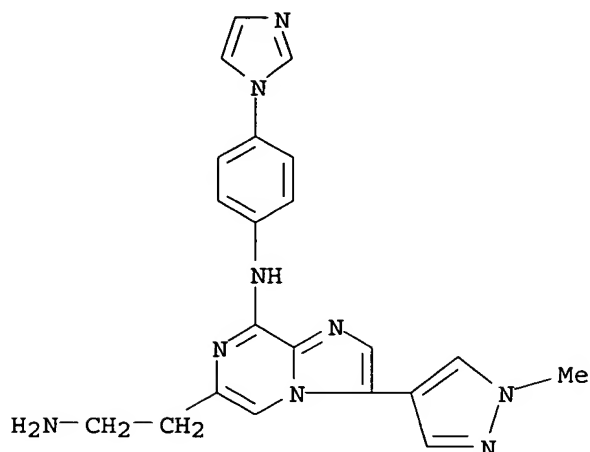
887476-03-1P 887476-38-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors useful in treatment and prevention of various diseases)

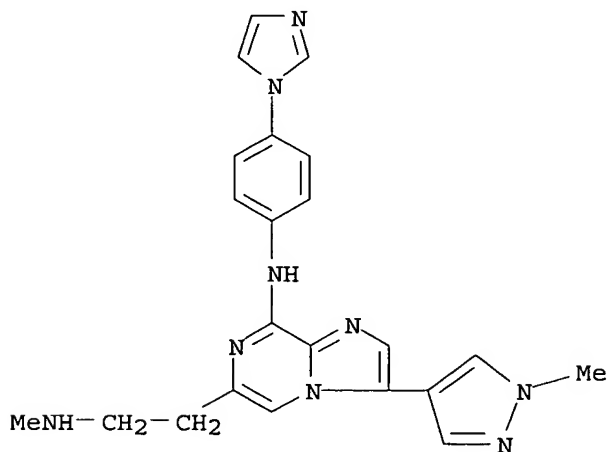
RN 887475-23-2 CAPLUS

CN Imidazo[1,2-a]pyrazine-6-ethanamine, 8-[[4-(1H-imidazol-1-yl)phenyl]amino]-3-(1-methyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



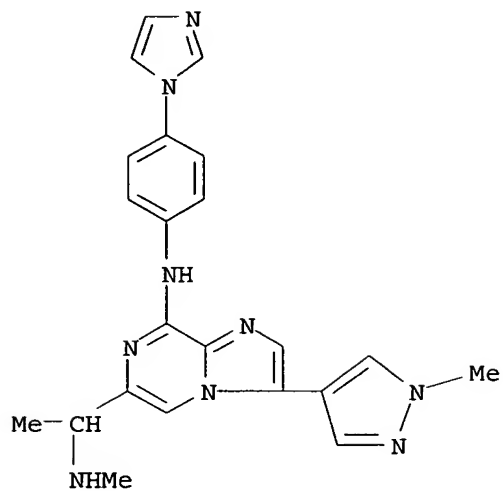
RN 887475-26-5 CAPLUS

CN Imidazo[1,2-a]pyrazine-6-ethanamine, 8-[[4-(1H-imidazol-1-yl)phenyl]amino]-N-methyl-3-(1-methyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



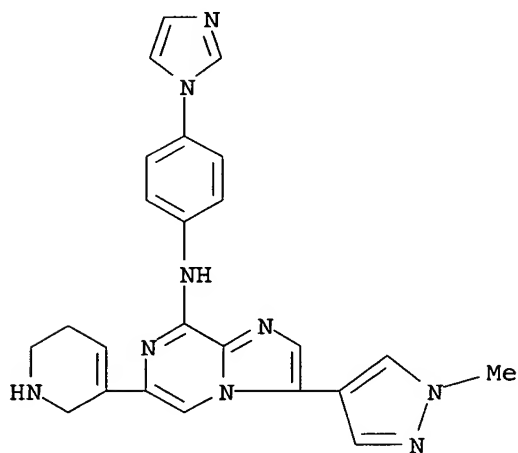
RN 887475-29-8 CAPLUS

CN Imidazo[1,2-a]pyrazine-6-methanamine, 8-[[4-(1H-imidazol-1-yl)phenyl]amino]-N,α-dimethyl-3-(1-methyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



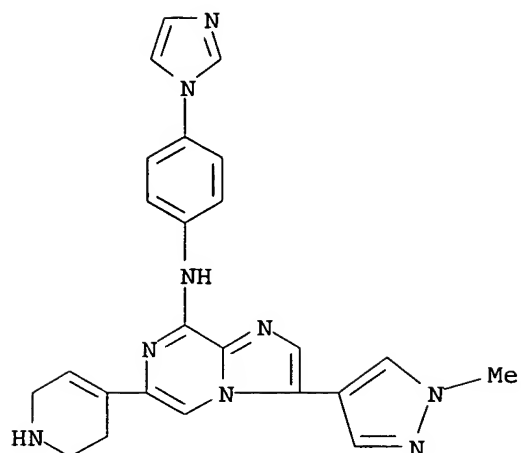
RN 887475-30-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(1H-imidazol-1-yl)phenyl]-3-(1-methyl-1H-pyrazol-4-yl)-6-(1,2,5,6-tetrahydro-3-pyridinyl)- (9CI) (CA INDEX NAME)



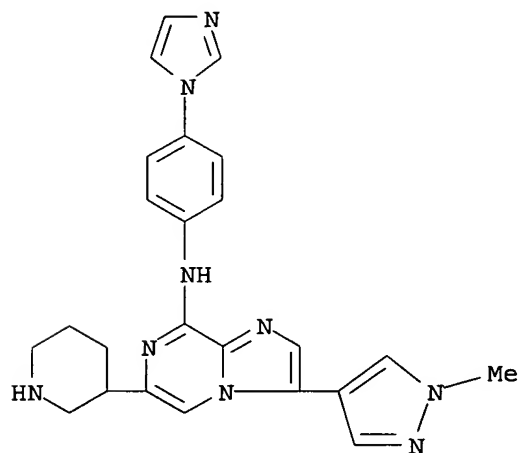
RN 887475-31-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(1H-imidazol-1-yl)phenyl]-3-(1-methyl-1H-pyrazol-4-yl)-6-(1,2,3,6-tetrahydro-4-pyridinyl)- (9CI) (CA INDEX NAME)



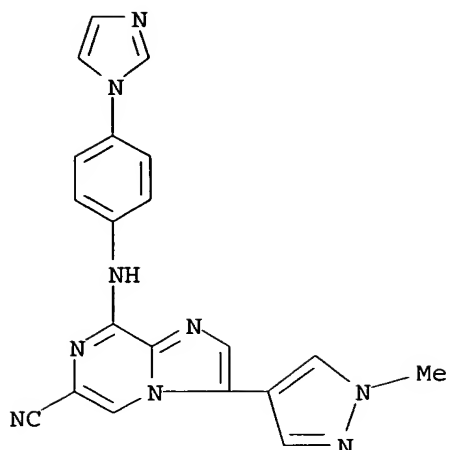
RN 887475-34-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(1H-imidazol-1-yl)phenyl]-3-(1-methyl-1H-pyrazol-4-yl)-6-(3-piperidinyl)- (9CI) (CA INDEX NAME)



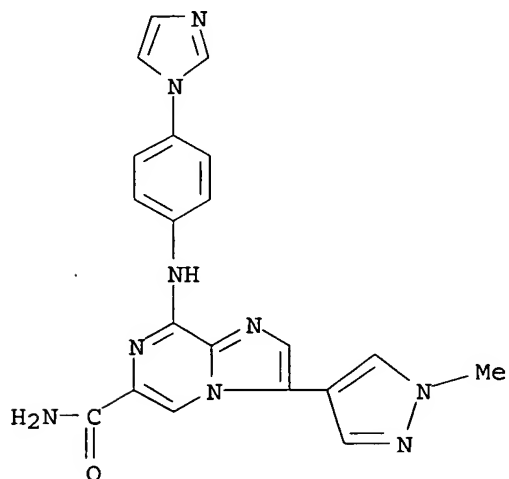
RN 887475-37-8 CAPLUS

CN Imidazo[1,2-a]pyrazine-6-carbonitrile, 8-[[4-(1H-imidazol-1-yl)phenyl]amino]-3-(1-methyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



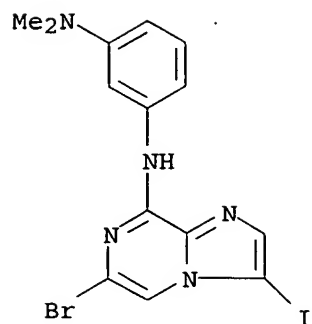
RN 887475-38-9 CAPLUS

CN Imidazo[1,2-a]pyrazine-6-carboxamide, 8-[[4-(1H-imidazol-1-yl)phenyl]amino]-3-(1-methyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



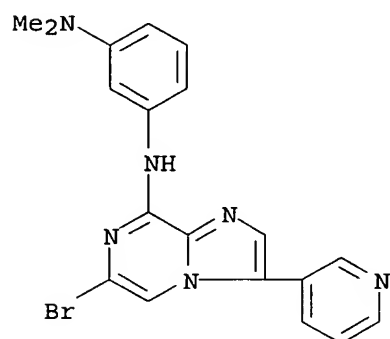
RN 887476-02-0 CAPLUS

CN 1,3-Benzenediamine, N'-(6-bromo-3-iodoimidazo[1,2-a]pyrazin-8-yl)-N,N-dimethyl- (9CI) (CA INDEX NAME)



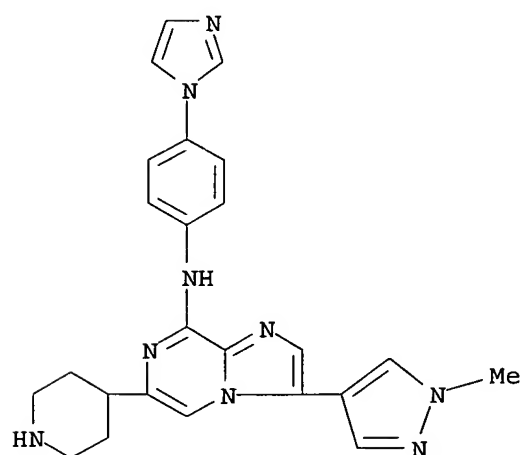
RN 887476-03-1 CAPLUS

CN 1,3-Benzenediamine, N'-[6-bromo-3-(3-pyridinyl)imidazo[1,2-a]pyrazin-8-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 887476-38-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(1H-imidazol-1-yl)phenyl]-3-(1-methyl-1H-pyrazol-4-yl)-6-(4-piperidinyl)- (9CI) (CA INDEX NAME)



IT 887475-77-6P 887475-82-3P 887475-87-8P

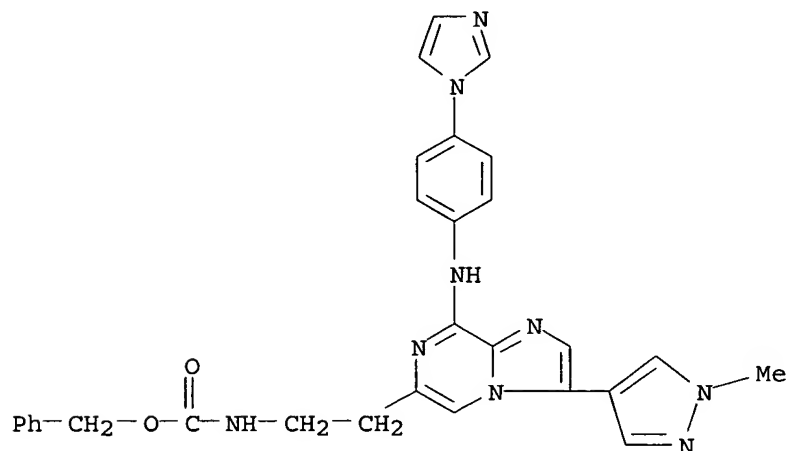
887475-88-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

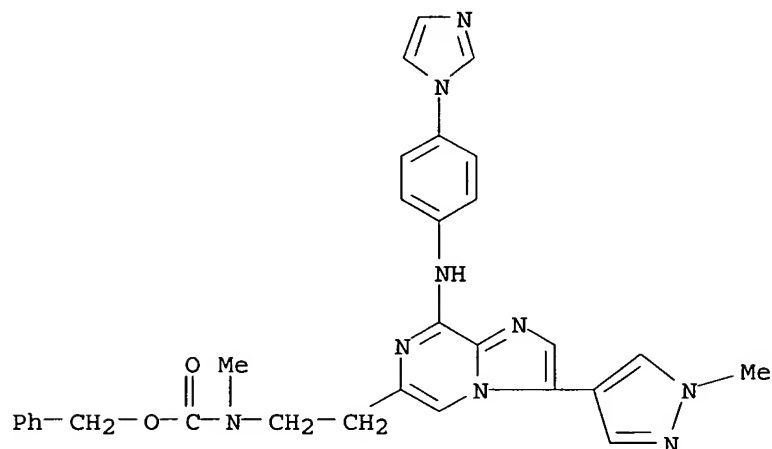
(preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors useful in treatment and prevention of various diseases)

RN 887475-77-6 CAPLUS

CN Carbamic acid, [2-[8-[[4-(1H-imidazol-1-yl)phenyl]amino]-3-(1-methyl-1H-pyrazol-4-yl)imidazo[1,2-a]pyrazin-6-yl]ethyl]-, phenylmethyl ester (9CI)
(CA INDEX NAME)

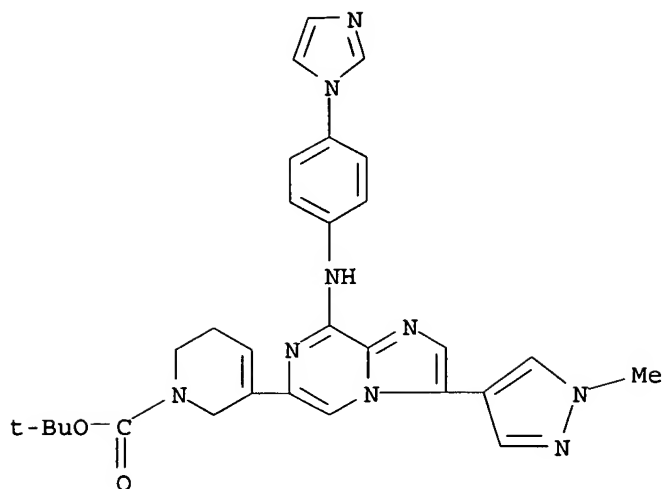
RN 887475-82-3 CAPLUS

CN Carbamic acid, [2-[8-[[4-(1H-imidazol-1-yl)phenyl]amino]-3-(1-methyl-1H-pyrazol-4-yl)imidazo[1,2-a]pyrazin-6-yl]ethyl]methyl-, phenylmethyl ester (9CI) (CA INDEX NAME)



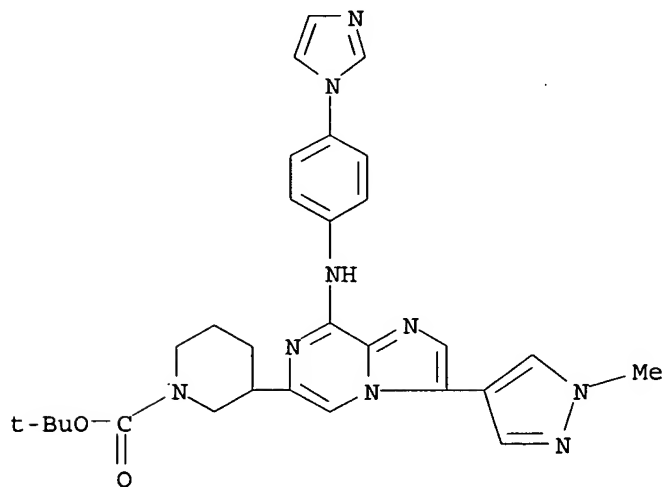
RN 887475-87-8 CAPLUS

CN 1(2H)-Pyridinecarboxylic acid, 5,6-dihydro-3-[8-[[4-(1H-imidazol-1-yl)phenyl]amino]-3-(1-methyl-1H-pyrazol-4-yl)imidazo[1,2-a]pyrazin-6-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 887475-88-9 CAPLUS

CN 1-Piperidinecarboxylic acid, 3-[8-[[4-(1H-imidazol-1-yl)phenyl]amino]-3-(1-methyl-1H-pyrazol-4-yl)imidazo[1,2-a]pyrazin-6-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L38 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:463188 CAPLUS

DOCUMENT NUMBER: 144:468207

TITLE: Imidazo[1,2-a]pyrazin-8-ylamines as Btk kinase inhibitors, their preparation, pharmaceutical compositions, and use in therapy

INVENTOR(S): Currie, Kevin, S.; Kropf, Jeffrey, E.; Darrow, James, W.; Desimone, Robert, W.

PATENT ASSIGNEE(S): Cgi Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2006053121	A2	20060518	WO 2005-US40730	20051110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2005288295	A1	20051229	US 2004-985023	20041110
PRIORITY APPLN. INFO.:			US 2004-985023	A 20041110
			US 2004-630645P	P 20041124
			US 2004-630860P	P 20041124
			US 2004-630861P	P 20041124
			US 2003-519311P	P 20031111

ED Entered STN: 18 May 2006

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

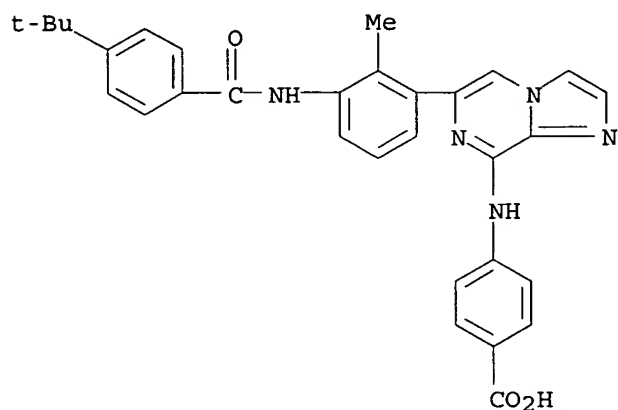
AB The invention relates to imidazo[1,2-a]pyrazin-8-ylamines I, which are inhibitors of Bruton's tyrosine kinase (Btk). In compds. I, R1 is (un)substituted phenylene or (un)substituted heteroarylene; L is a bond, -O-, (un)substituted C1-4 alkylene, -O-(un)substituted C1-4 alkylene-, -C(O)-, etc.; G is H, OH, halo, nitro, alkoxy, (un)substituted alkyl, (un)substituted amino, (un)substituted heterocyclyl, (un)substituted cycloalkyl, (un)substituted aryl, or (un)substituted heteroaryl; T, V, and W are selected from C(R2) and N, where each R2 is independently selected from H, OH, halo, (un)substituted lower alkyl, and (un)substituted lower alkoxy; U is CH or N; Q is (un)substituted methyleneamino, (un)substituted aminomethylene, (un)substituted aminocarbonyl, (un)substituted carbonylamino, or (un)substituted ureido; A is a bond or -CH=CH-; R5 is (un)substituted cycloalkyl, (un)substituted heterocyclyl, (un)substituted aryl, or (un)substituted heteroaryl; and R6 is H, (un)substituted alkyl, cycloalkyl, or heterocyclyl; provided that at most one of T, U, V, and W is N. The invention also relates to the prepn of I, pharmaceutical compns. comprising at least one compound I, together with at least one pharmaceutically acceptable vehicle chosen from carriers, adjuvants, and excipients, as well as to the use of the compns. for the treatment of diseases responsive to inhibition of Btk activity, such as cancer. Borination of 1-bromo-2-methyl-3-nitrobenzene with bis(neopentyl glycolato)diboron followed by hydrogenation and amidation with 4-tert-butylbenzoyl chloride gave dioxaborinane II, which underwent Suzuki coupling with bromoimidazopyrazine III, ester hydrolysis and amidation with morpholine to give imidazopyrazinylamine IV. Some compds. of the invention express IC50 values below 0.1 μ M in a Btk biochem. assay and below 10 μ M in at least one of four cell-based assays (no specific data).

IT 852221-24-0P, 4-[6-[3-(4-tert-Butylbenzoylamino)-2-

methylphenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid
852221-26-2P, 4-[6-[3-(4-tert-Butylbenzoylamino)-2-methylphenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid ethyl ester
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (drug candidate; preparation of imidazopyrazinylamines as Btk kinase inhibitors)

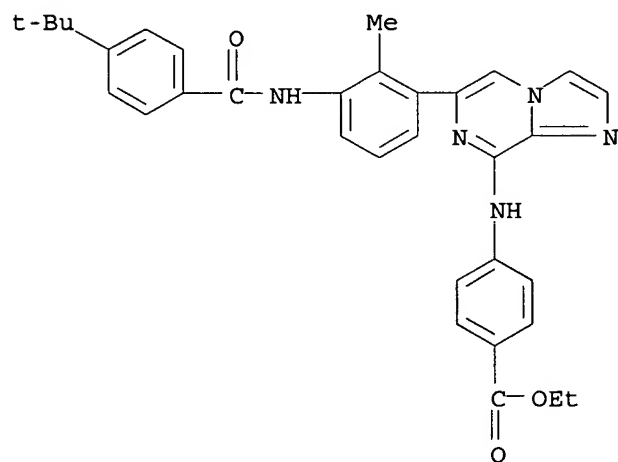
RN 852221-24-0 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



RN 852221-26-2 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



IT **852221-23-9P**, 4-[6-[3-(4-tert-Butylbenzoylamino)-4-

methylphenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid

852221-25-1P, 4-[[6-[5-((4-tert-Butylbenzoyl)amino)-2-

methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid

852221-27-3P, 4-tert-Butyl-N-[2-methyl-5-[8-(4-sulfamoylphenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide

886854-77-9P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(morpholine-4-carbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide
886854-82-6P, 6-tert-Butyl-N-[2-methyl-3-[8-((4-(morpholin-4-yl)methyl)phenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]nicotinamide
886854-89-3P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide
886854-90-6P, N-[5-[8-[4-(4-Acetylpiperazin-1-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-tert-butylbenzamide 886854-91-7P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(N-methyl-N-(2-hydroxyethyl)carbamoyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886854-92-8P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(N,N-dimethylcarbamoyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886854-93-9P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(N-methylcarbamoyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886854-94-0P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-carbamoylphenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886854-95-1P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(4-methylpiperazin-1-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886854-96-2P, N-[5-[8-[4-(4-Acetylpiperazin-1-yl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-tert-butylbenzamide 886854-97-3P, 4-tert-Butyl-N-[2-fluoro-5-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886854-98-4P, 4-tert-Butyl-N-[2-methyl-5-[8-((4-(morpholin-4-yl)methyl)phenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886854-99-5P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(3-oxopiperazin-1-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-00-1P, N-[5-[8-[4-(4-Acetylpiperazin-1-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-tert-butylbenzamide 886855-03-4P, 4-tert-Butyl-N-[5-[8-[4-((5,6-dihydro-8H-imidazo[1,2-a]pyrazin-7-yl)methyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]benzamide 886855-06-7P, [4-[6-[3-((4-tert-Butylbenzoyl)amino)-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]acetic acid 886855-08-9P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(2-(morpholin-4-yl)-2-oxoethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-09-0P, 4-tert-Butyl-N-[5-[8-[4-[N-(2-hydroxyethyl)-N-methylcarbamoyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]benzamide 886855-10-3P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-[2-(4-methylpiperazin-1-yl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-11-4P, [3-[6-[3-((4-tert-Butylbenzoyl)amino)-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]acetic acid 886855-12-5P, 4-tert-Butyl-N-[2-methyl-5-[8-[3-(2-(morpholin-4-yl)-2-oxoethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-13-6P, 4-tert-Butyl-N-[2-methyl-5-[8-[3-[2-(4-methylpiperazin-1-yl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-14-7P, 4-tert-Butyl-N-[5-[8-((3-((dimethylcarbamoyl)methyl)phenyl)amino]imidazo[1,2-a]pyrazin-6-yl)-2-methylphenyl]benzamide 886855-15-8P, 2-[3-[6-[3-((4-tert-Butylbenzoyl)amino)-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]propionic acid 886855-16-9P, 4-[6-[3-((4-tert-Butylbenzoyl)amino)-4-methoxyphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid 886855-17-0P, 4-tert-Butyl-N-[2-methyl-5-[8-[4-(1-methyl-2-(morpholin-4-yl)-2-oxoethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-18-1P, 4-[6-[3-((4-tert-Butylbenzoyl)amino)-4-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid 886855-19-2P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(4-methylpiperazin-1-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]benzamide

886855-20-5P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(N-methyl-N-(2-hydroxyethyl)amino)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]benzamide 886855-21-6P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(N-methyl-N-ethylamino)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]benzamide 886855-22-7P, 4-tert-Butyl-N-[4-methyl-3-[8-[4-(N-methyl-N-(2-hydroxyethyl)amino)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]benzamide 886855-23-8P, 4-tert-Butyl-N-[2-fluoro-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-24-9P, 6-tert-Butyl-N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]nicotinamide 886855-25-0P, 1,2,3-Thiadiazole-4-carboxamide N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] 886855-26-1P, Isoxazole-5-carboxamide N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] 886855-27-2P, Pyridine-2-carboxamide N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl] 886855-28-3P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(4-(morpholin-4-yl)methyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-29-4P, 4-Isopropyl-N-[2-methyl-3-[8-[4-(4-(morpholin-4-yl)methyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-30-7P, 6-Hydroxy-N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]nicotinamide 886855-31-8P, 5-tert-Butyloxazole-2-carboxamide N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] 886855-32-9P, N-[2-Methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(methylsulfanyl)benzamide 886855-33-0P, 4-(1H-Imidazol-2-yl)-N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-34-1P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(1H-tetrazol-5-yl)-phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-35-2P, 4-(Methanesulfonyl)-N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]benzamide 886855-36-3P, 2-Hydroxy-6-methyl-N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]nicotinamide 886855-37-4P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(1H-tetrazol-5-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-38-5P, 2,5-Dimethyl-2H-pyrazole-3-carboxamide N-[2-methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] 886855-39-6P, N-[2-Methyl-3-[8-[4-(morpholin-4-ylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]nicotinamide 886855-40-9P 886855-41-0P, N-[3-[8-(3-Aminophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-tert-butylbenzamide 886855-42-1P, Tetrahydrofuran-2-carboxamide N-[3-[6-[3-(4-tert-butylbenzoyl)amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl] 886855-43-2P, 4-tert-Butyl-N-[2-methyl-3-[8-[4-(N-methylcarbamimidoyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-48-7P, 4-tert-Butyl-N-[3-[8-(4-carbamimidoylphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]benzamide 886855-49-8P, 4-tert-Butyl-N-[3-[8-[4-(N,N'-dimethylcarbamimidoyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-50-1P, 4-tert-Butyl-N-[3-[8-[4-(imino)(morpholin-4-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-phenyl]benzamide 886855-51-2P, 4-tert-Butyl-N-[3-[8-[4-(N,N'-dimethylcarbamimidoyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide 886855-52-3P, 4-tert-Butyl-N-[3-[8-[4-(2-imino-2-(morpholin-4-yl)ethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]benzamide 886855-53-4P, 4-tert-Butyl-N-[3-[8-[4-(N,N'-dimethylcarbamimidoyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-

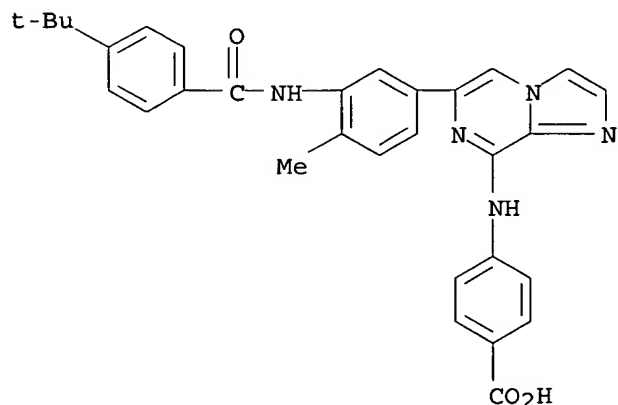
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of imidazopyrazinylamines as Btk kinase inhibitors)

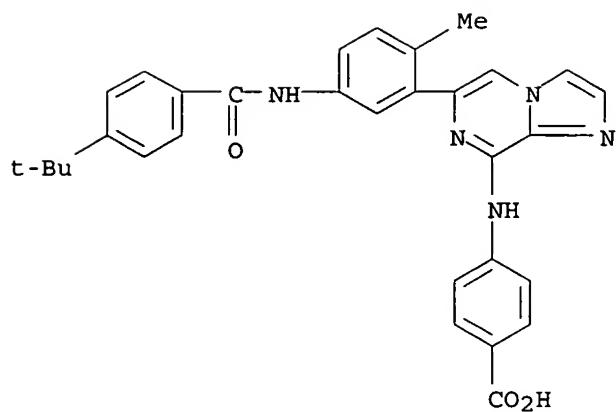
RN 852221-23-9 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



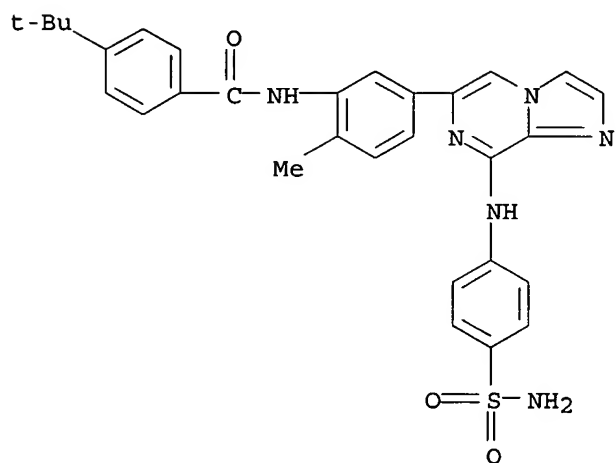
RN 852221-25-1 CAPLUS

CN Benzoic acid, 4-[[6-[5-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



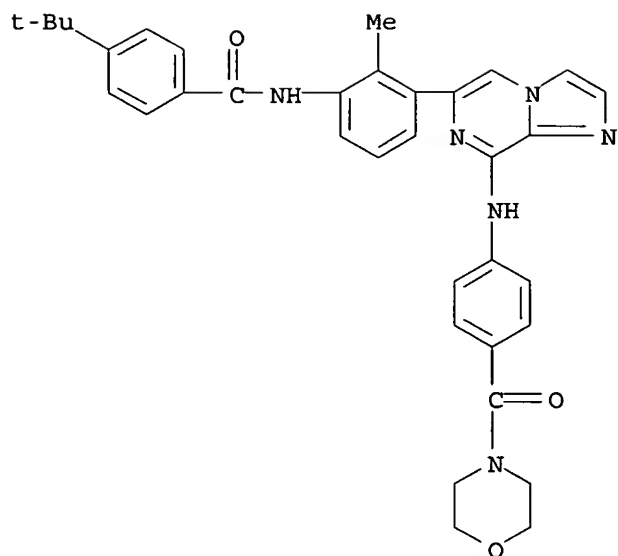
RN 852221-27-3 CAPLUS

CN Benzamide, N-[5-[8-[[4-(aminosulfonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



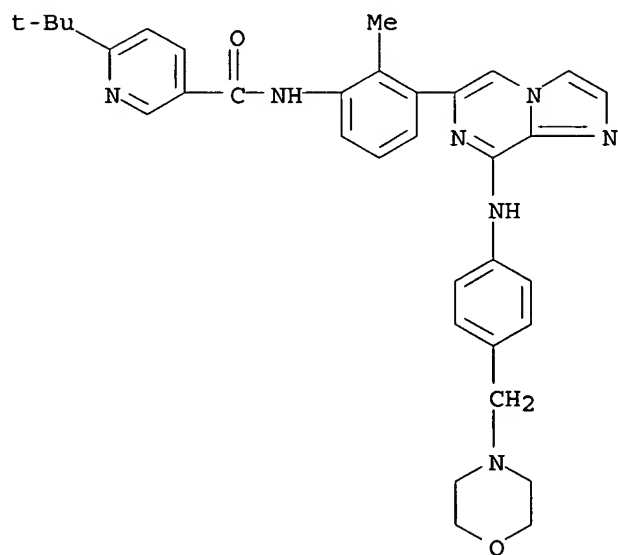
RN 886854-77-9 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



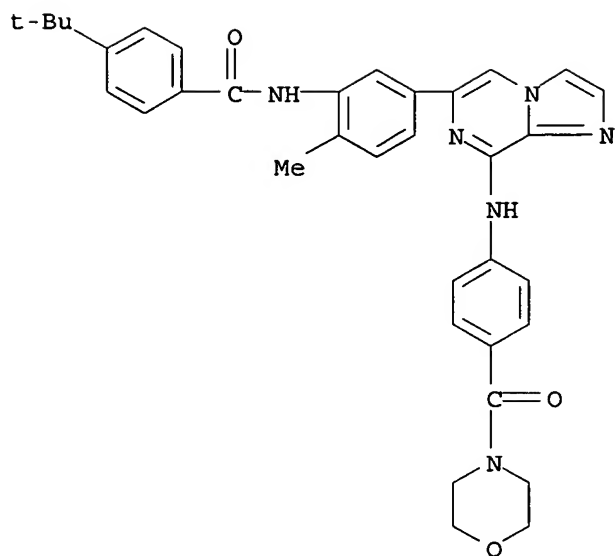
RN 886854-82-6 CAPLUS

CN 3-Pyridinecarboxamide, 6-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-(4-morpholinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



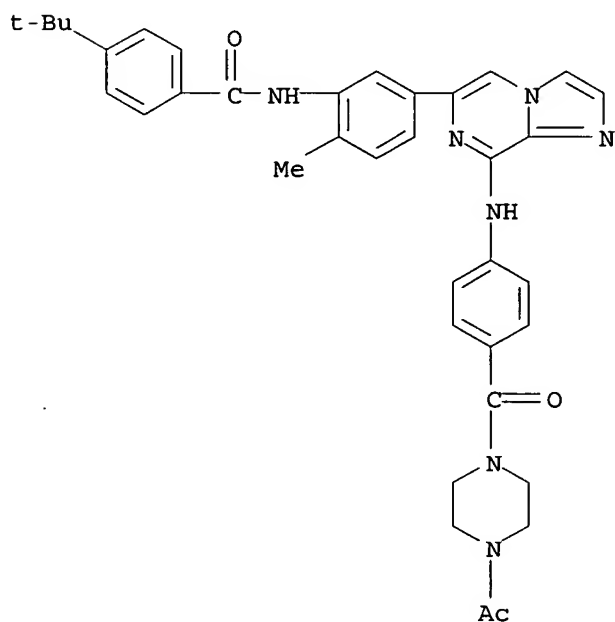
RN 886854-89-3 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-5-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



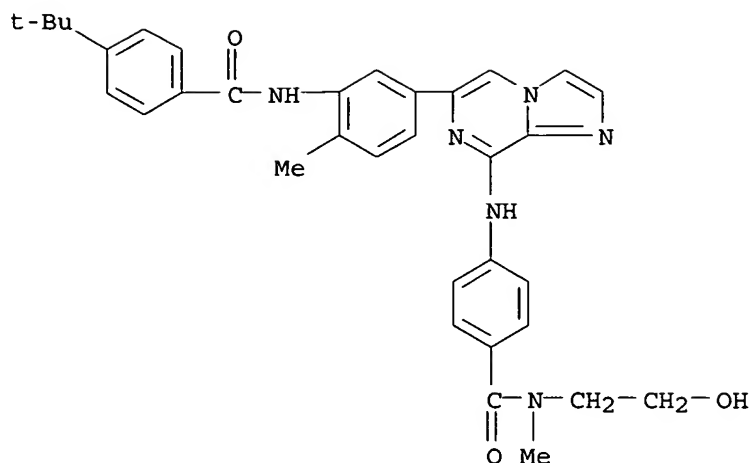
RN 886854-90-6 CAPLUS

CN Benzamide, N- [5- [8- [[4- [(4-acetyl-1-piperazinyl) carbonyl] phenyl] amino] imidazo [1,2-a] pyrazin-6-yl] -2-methylphenyl] -4- (1,1-dimethylethyl) - (9CI) (CA INDEX NAME)



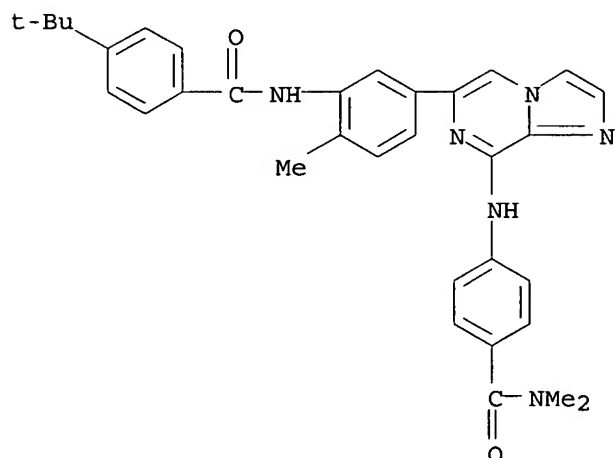
RN 886854-91-7 CAPLUS

CN Benzamide, 4- [[6- [3- [[4- (1,1-dimethylethyl) benzoyl] amino] -4-methylphenyl] imidazo [1,2-a] pyrazin-8-yl] amino] -N- (2-hydroxyethyl) -N-methyl- (9CI) (CA INDEX NAME)



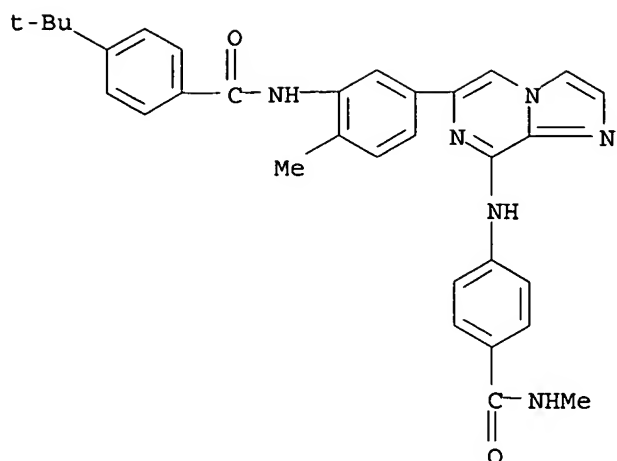
RN 886854-92-8 CAPLUS

CN Benzamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl- (9CI) (CA INDEX NAME)



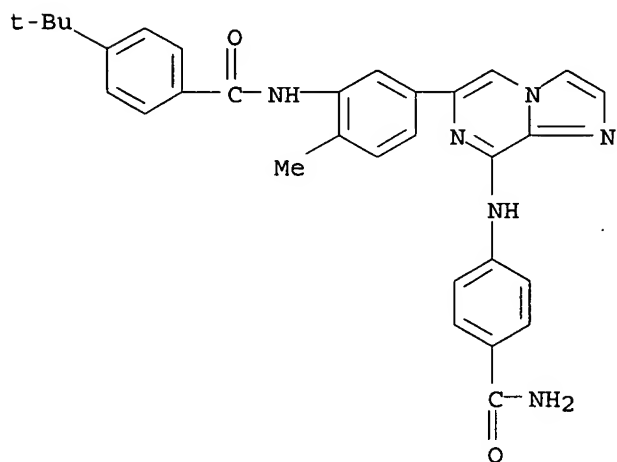
RN 886854-93-9 CAPLUS

CN Benzamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl- (9CI) (CA INDEX NAME)



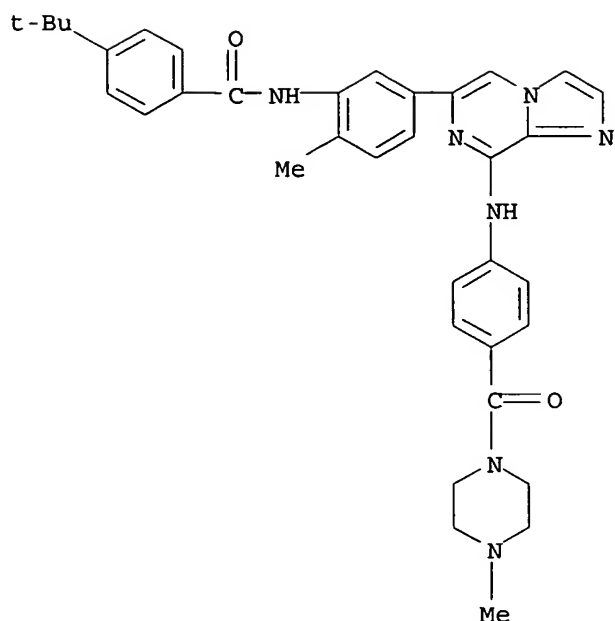
RN 886854-94-0 CAPLUS

CN Benzamide, N-[5-[8-[[4-(aminocarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



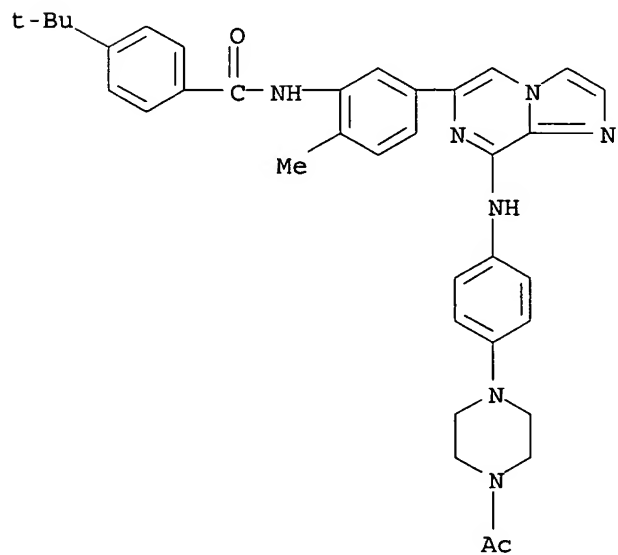
RN 886854-95-1 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-5-[8-[[4-[(4-methyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



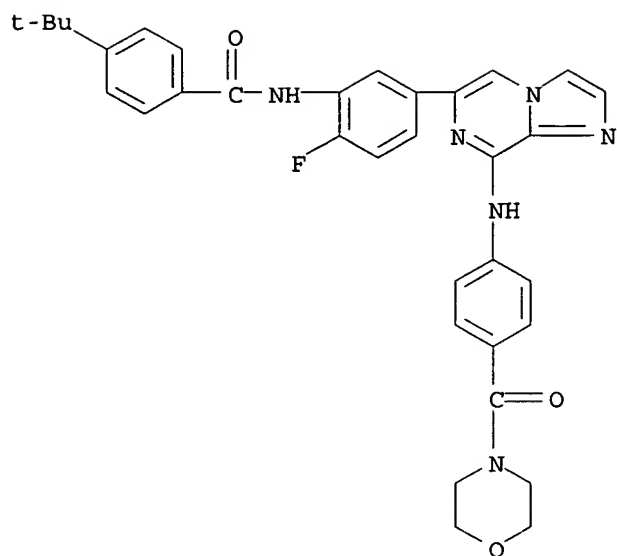
RN 886854-96-2 CAPLUS

CN Benzamide, N-[5-[8-[[4-(4-acetyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



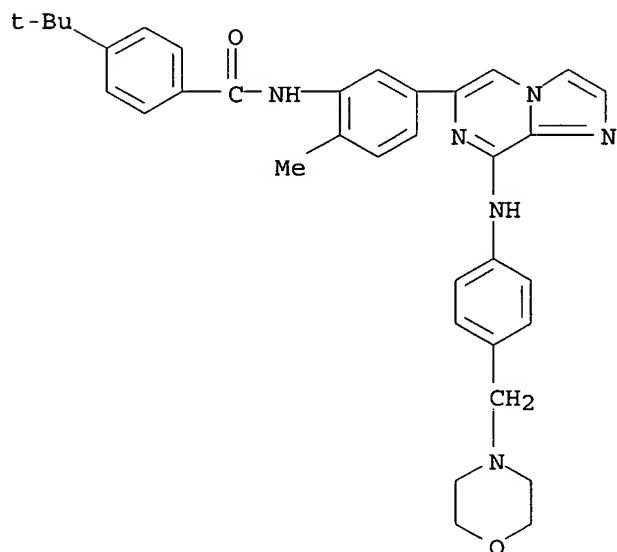
RN 886854-97-3 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-fluoro-5-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



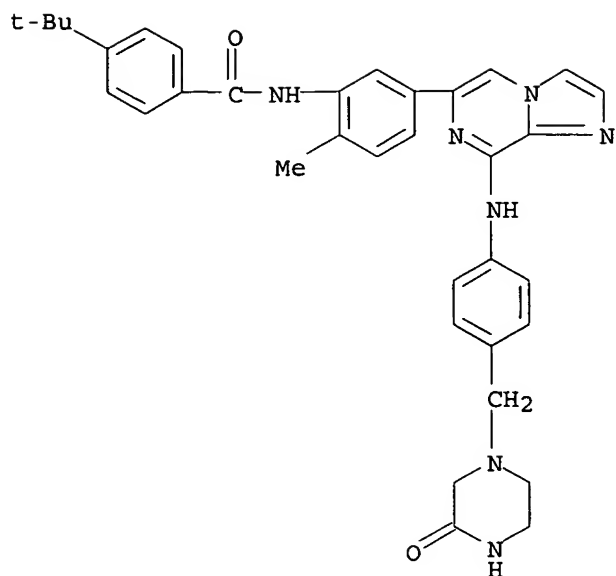
RN 886854-98-4 CAPLUS

CN Benzamide, 4- (1,1-dimethylethyl) -N- [2-methyl-5- [8- [[4- (4-morpholinylmethyl) phenyl] amino] imidazo [1,2-a] pyrazin-6-yl] phenyl] - (9CI)
(CA INDEX NAME)



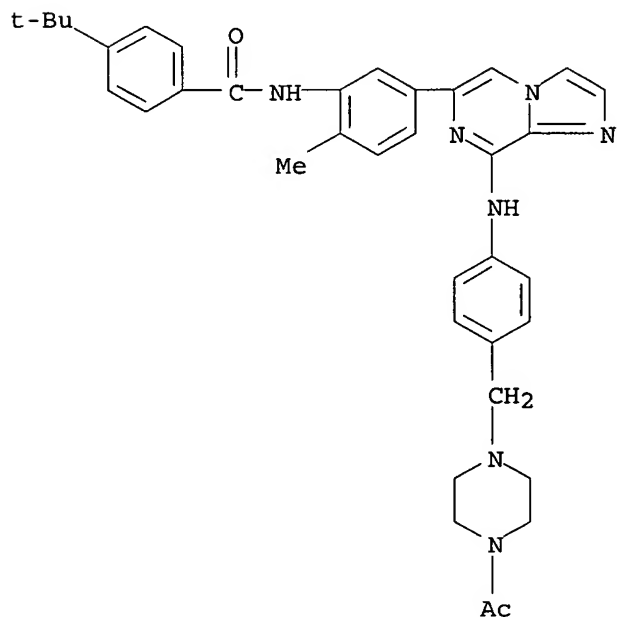
RN 886854-99-5 CAPLUS

CN Benzamide, 4- (1,1-dimethylethyl) -N- [2-methyl-5- [8- [[4- [(3-oxo-1-piperazinyl) methyl] phenyl] amino] imidazo [1,2-a] pyrazin-6-yl] phenyl] - (9CI)
(CA INDEX NAME)



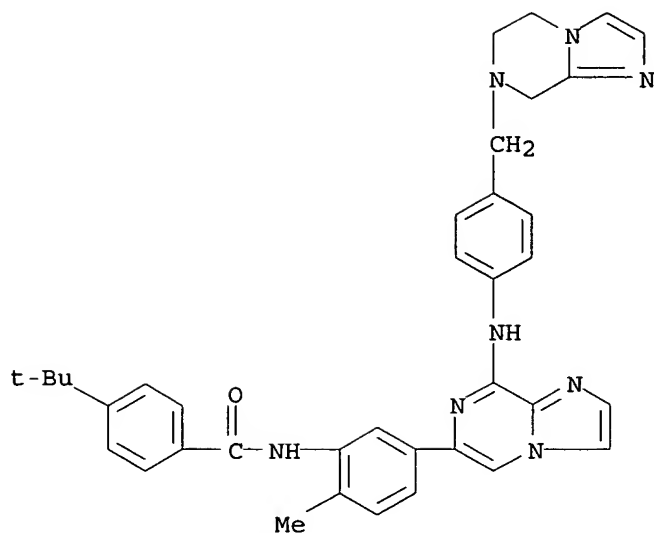
RN 886855-00-1 CAPLUS

CN Benzamide, N-[5-[8-[[4-[(4-acetyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)-(9CI) (CA INDEX NAME)



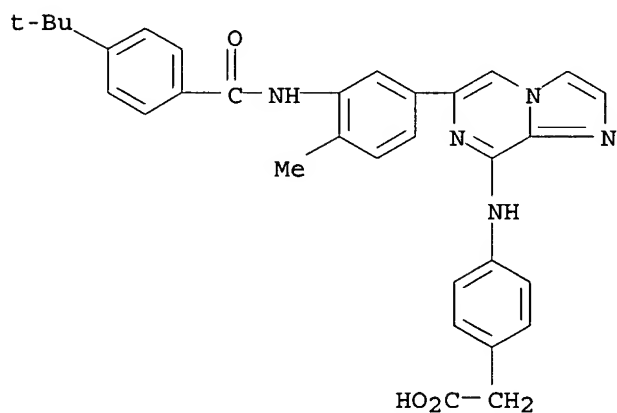
RN 886855-03-4 CAPLUS

CN Benzamide, N-[5-[8-[[4-[(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)-(9CI) (CA INDEX NAME)



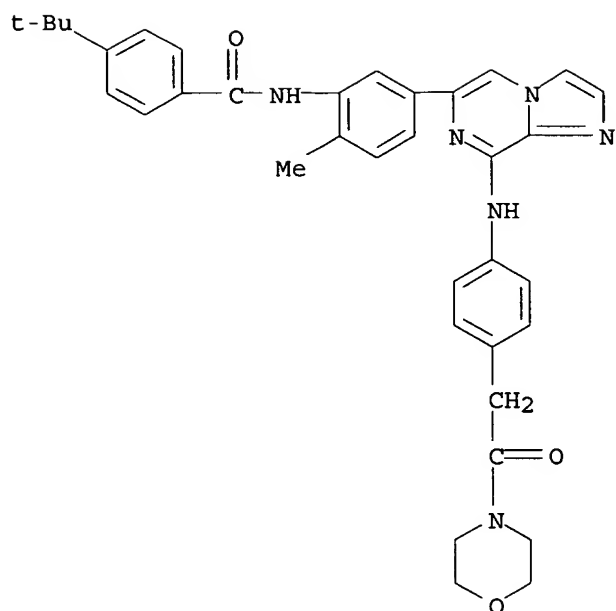
RN 886855-06-7 CAPLUS

CN Benzeneacetic acid, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-phenyl]pyrazin-6-yl]phenyl]-2-oxoethyl]benzamide, 4-(1,1-dimethylethyl)-N- (9CI) (CA INDEX NAME)



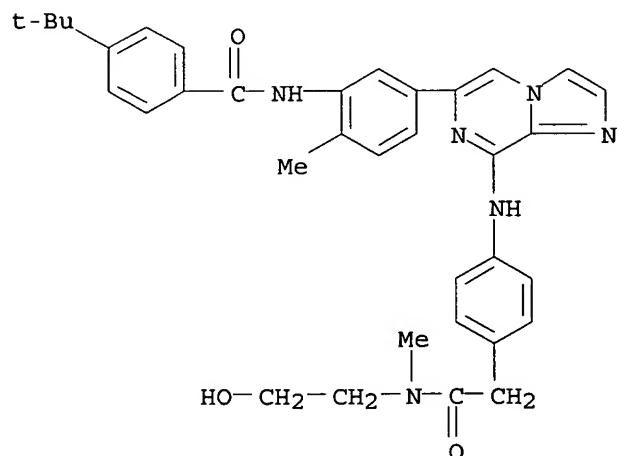
RN 886855-08-9 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-5-[8-[[4-[2-(4-morpholinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-2-oxoethyl]benzamide, 4-(1,1-dimethylethyl)-N- (9CI) (CA INDEX NAME)



RN 886855-09-0 CAPLUS

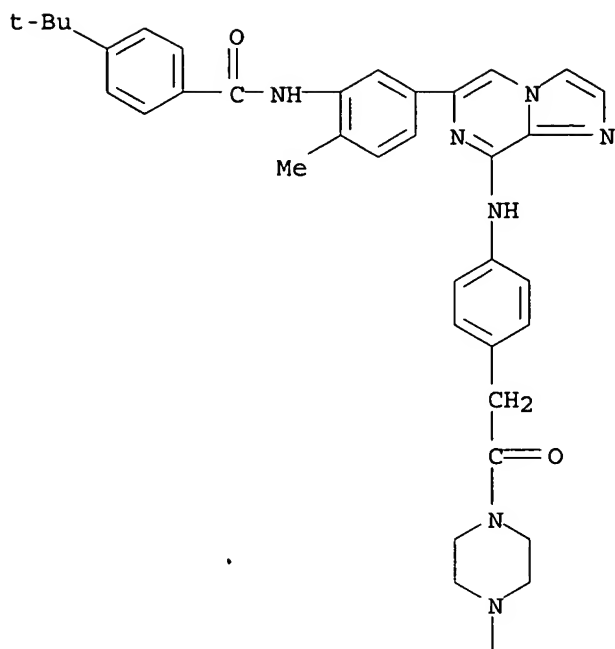
CN Benzeneacetamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)-N-methyl-
(9CI) (CA INDEX NAME)



RN 886855-10-3 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-5-[8-[[4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-
(9CI) (CA INDEX NAME)

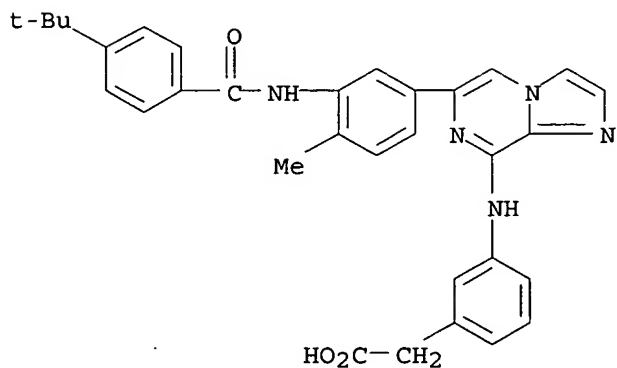
PAGE 1-A



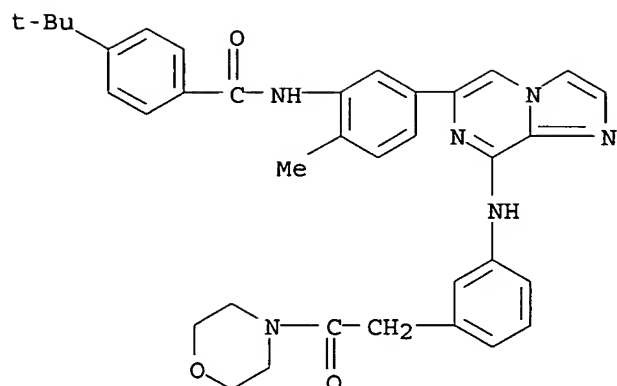
PAGE 2-A



RN 886855-11-4 CAPLUS
 CN Benzeneacetic acid, 3-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)

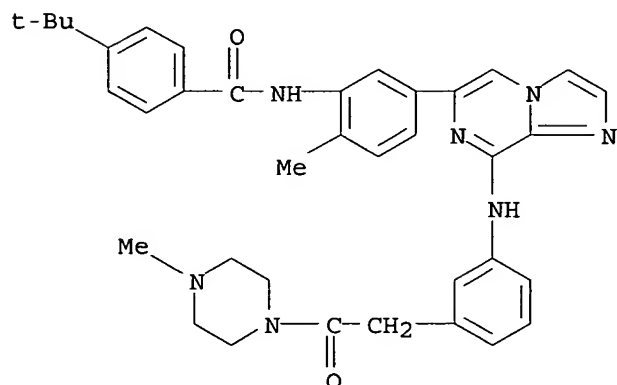


RN 886855-12-5 CAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-5-[8-[[3-[2-(4-morpholinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



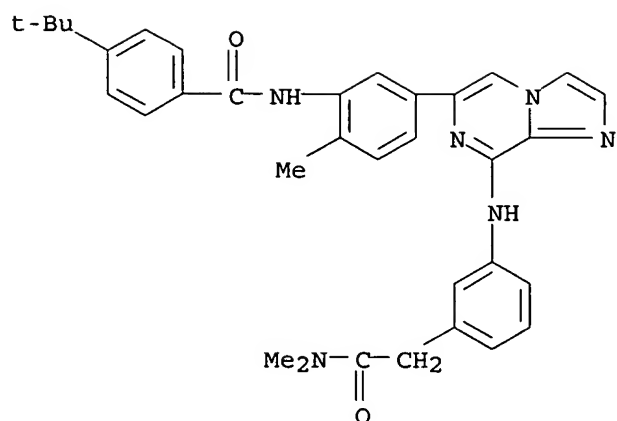
RN 886855-13-6 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-5-[8-[[3-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



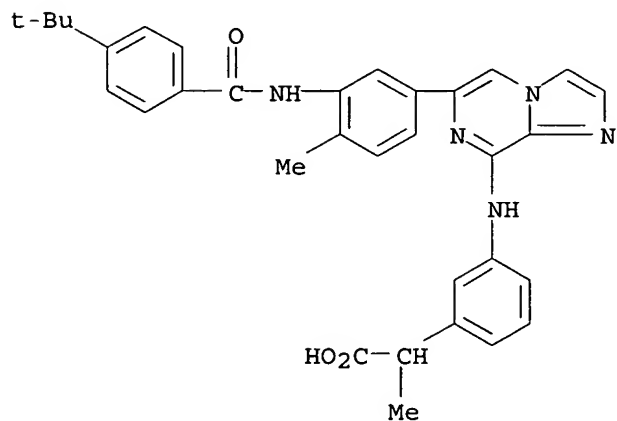
RN 886855-14-7 CAPLUS

CN Benzeneacetamide, 3-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl-(9CI) (CA INDEX NAME)



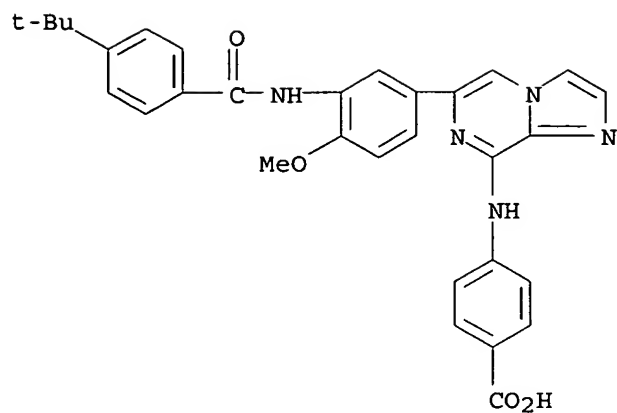
RN 886855-15-8 CAPLUS

CN Benzeneacetic acid, 3-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- α -methyl- (9CI) (CA INDEX NAME)



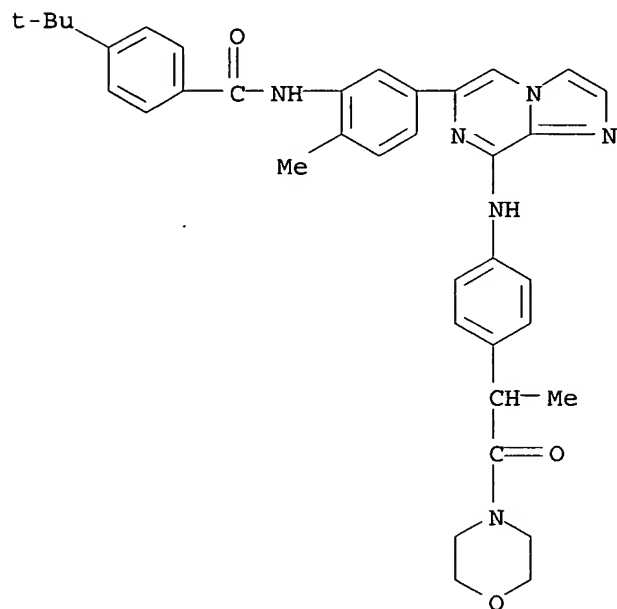
RN 886855-16-9 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methoxyphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



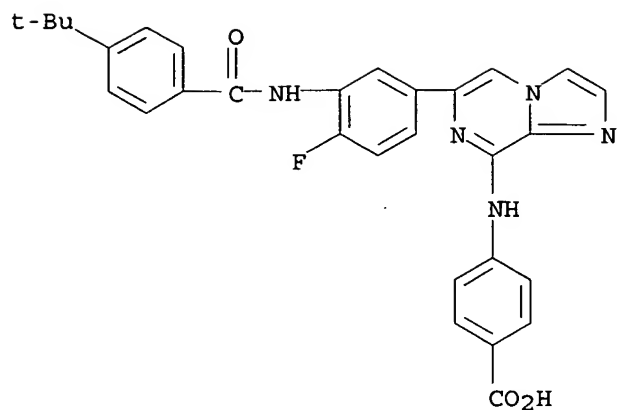
RN 886855-17-0 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-5-[8-[[4-[1-methyl-2-(4-morpholinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



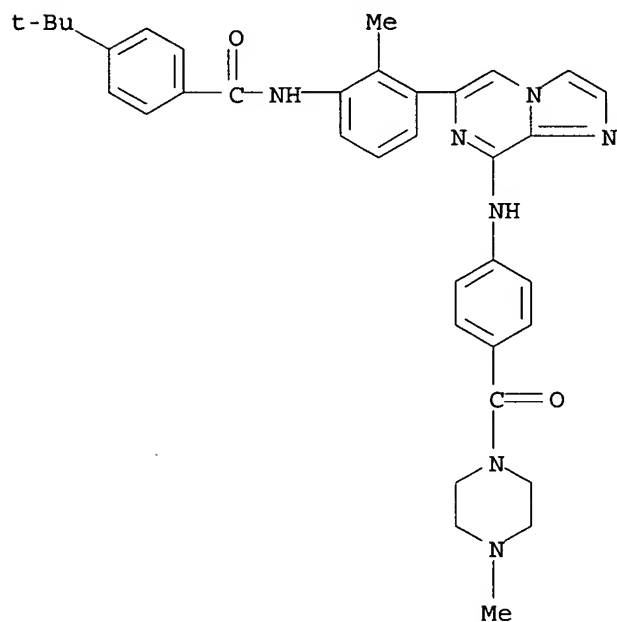
RN 886855-18-1 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-(9CI) (CA INDEX NAME)



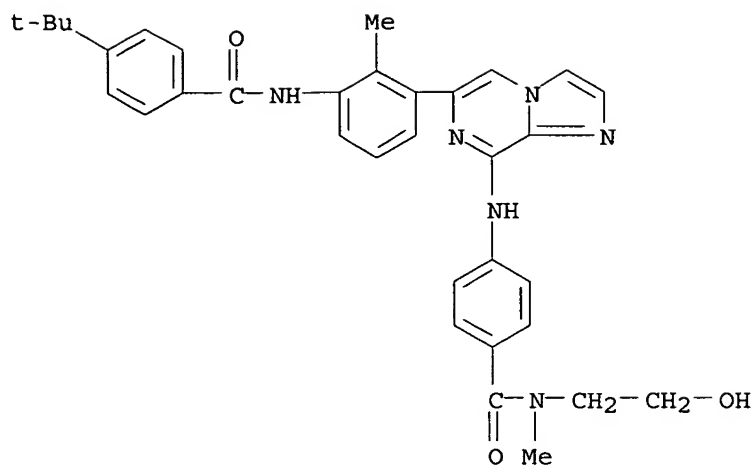
RN 886855-19-2 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-[(4-methyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



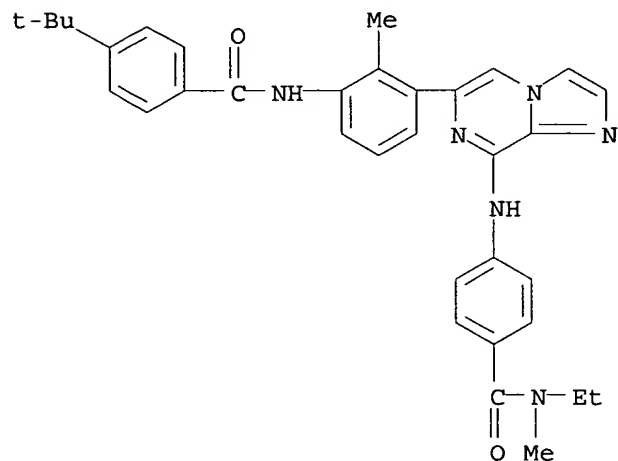
RN 886855-20-5 CAPLUS

CN Benzamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)-N-methylpiperazine-1-carboxamide (9CI) (CA INDEX NAME)



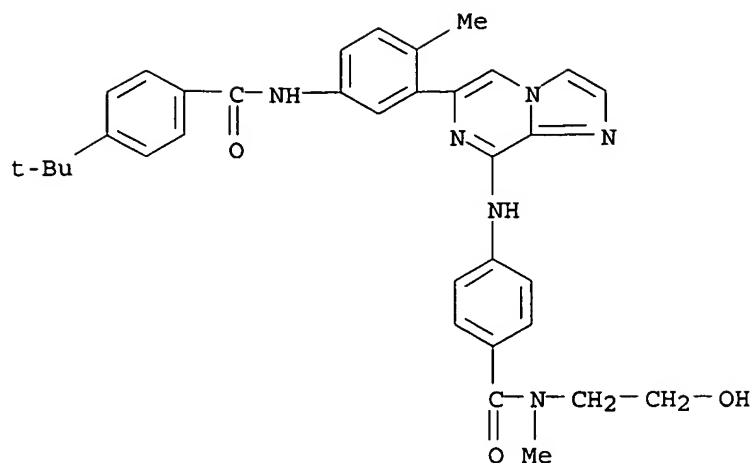
RN 886855-21-6 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-ethyl-N-methyl-2-hydroxyethyl]benzamide (9CI)
(CA INDEX NAME)



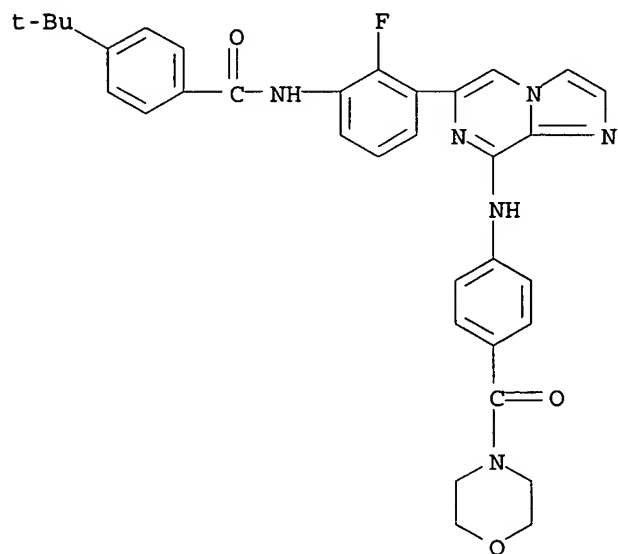
RN 886855-22-7 CAPLUS

CN Benzamide, 4-[[6-[[5-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)-N-methyl-2-ethyl]benzamide (9CI)
(CA INDEX NAME)



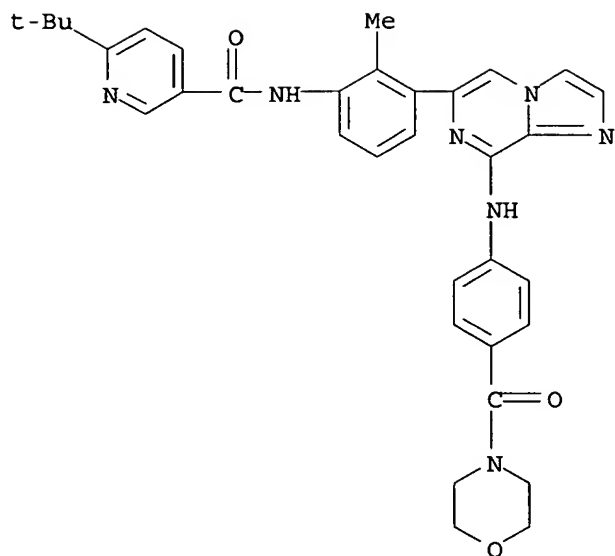
RN 886855-23-8 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-fluoro-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



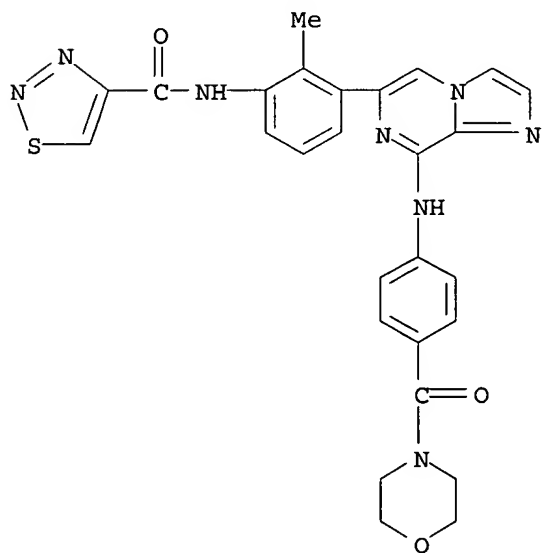
RN 886855-24-9 CAPLUS

CN 3-Pyridinecarboxamide, 6-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



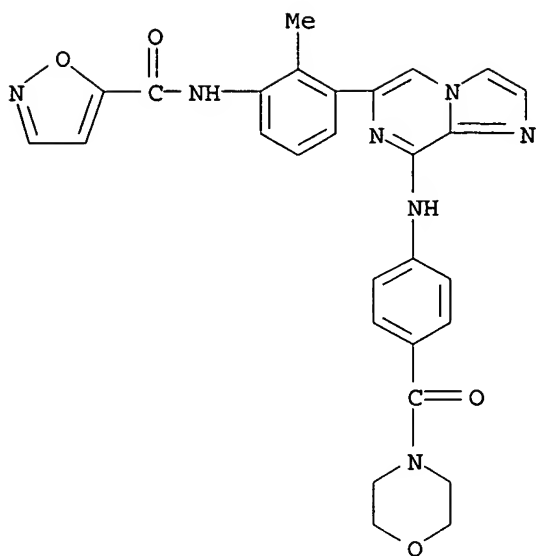
RN 886855-25-0 CAPLUS

CN 1,2,3-Thiadiazole-4-carboxamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



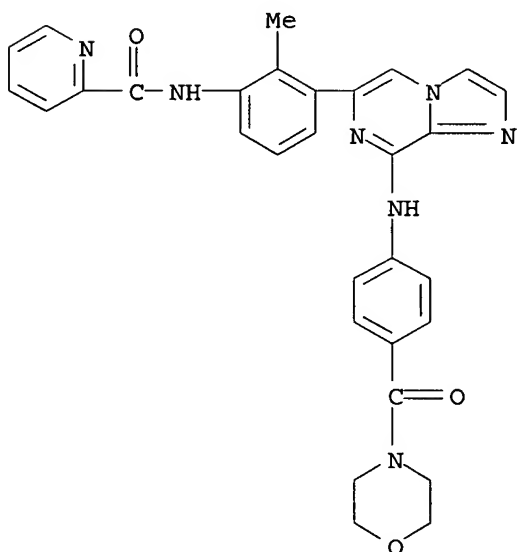
RN 886855-26-1 CAPLUS

CN 5-Isoxazolecarboxamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



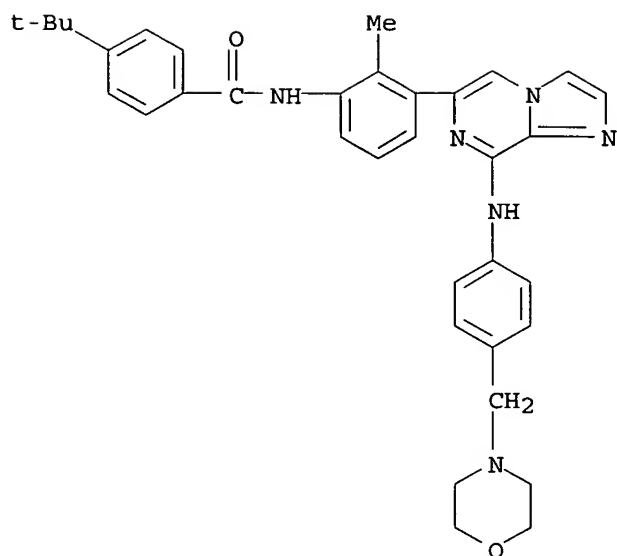
RN 886855-27-2 CAPLUS

CN 2-Pyridinecarboxamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



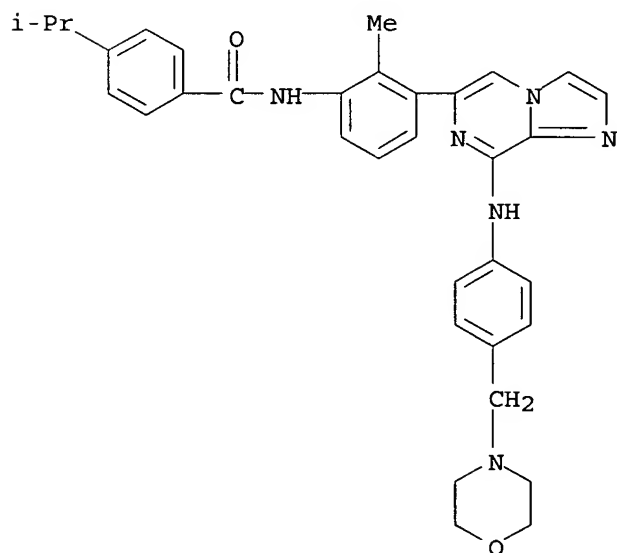
RN 886855-28-3 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-(4-morpholinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



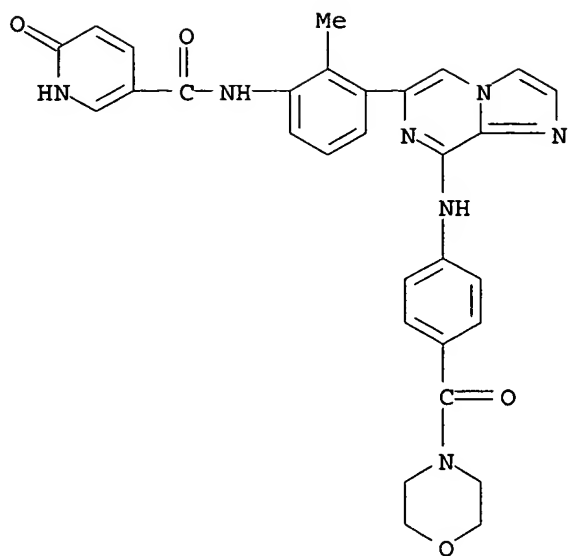
RN 886855-29-4 CAPLUS

CN Benzamide, 4-(1-methylethyl)-N-[2-methyl-3-[8-[[4-(4-morpholinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



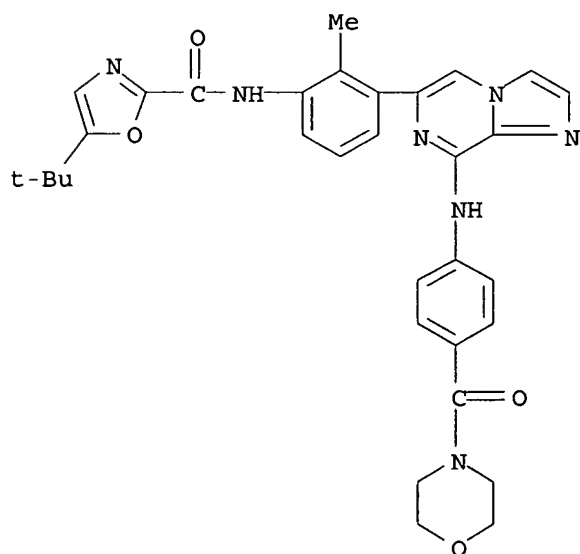
RN 886855-30-7 CAPLUS

CN 3-Pyridinecarboxamide, 1,6-dihydro-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] -6-oxo- (9CI) (CA INDEX NAME)



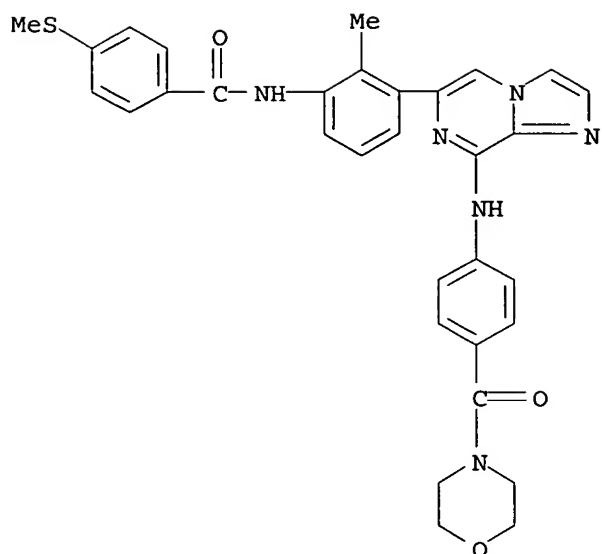
RN 886855-31-8 CAPLUS

CN 2-Oxazolecaboxamide, 5-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



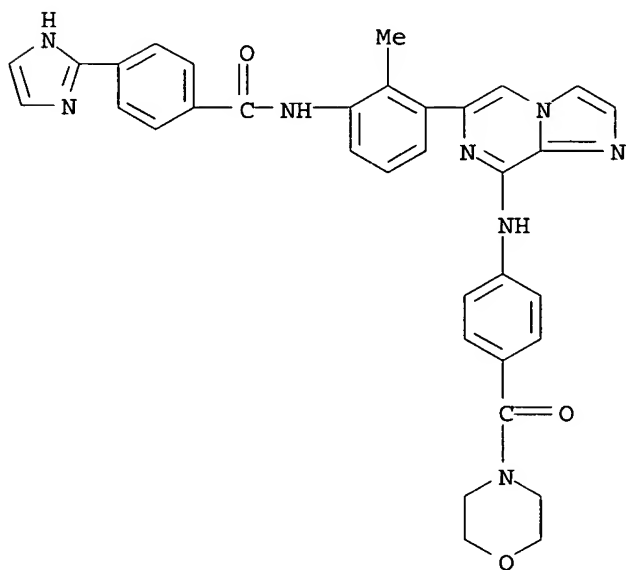
RN 886855-32-9 CAPLUS

CN Benzamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(methylthio)- (9CI) (CA INDEX NAME)



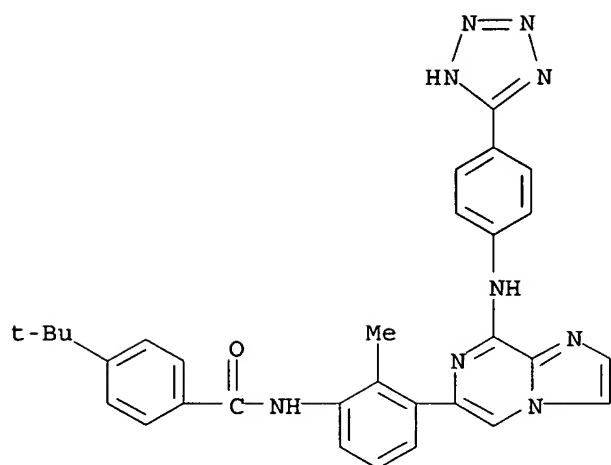
RN 886855-33-0 CAPLUS

CN Benzamide, 4-(1H-imidazol-2-yl)-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



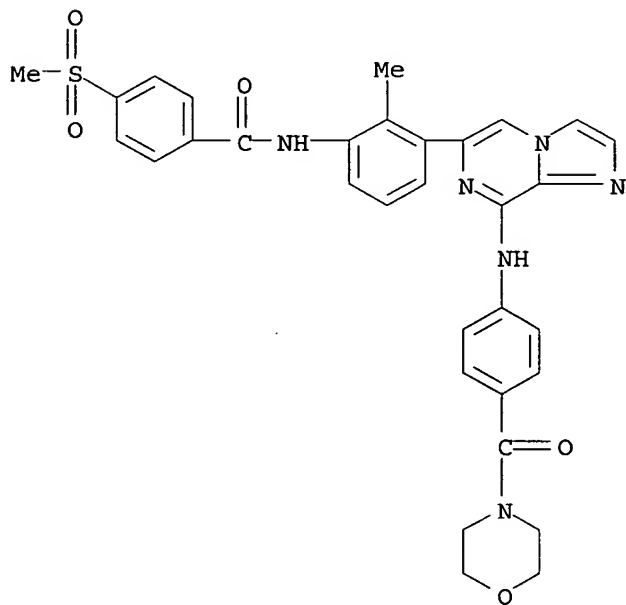
RN 886855-34-1 CAPLUS

CN INDEX NAME NOT YET ASSIGNED



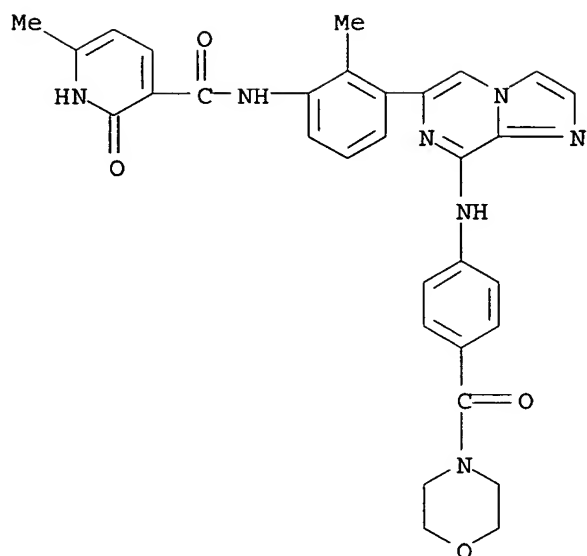
RN 886855-35-2 CAPLUS

CN Benzamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(methanesulfonyl)- (9CI) (CA INDEX NAME)

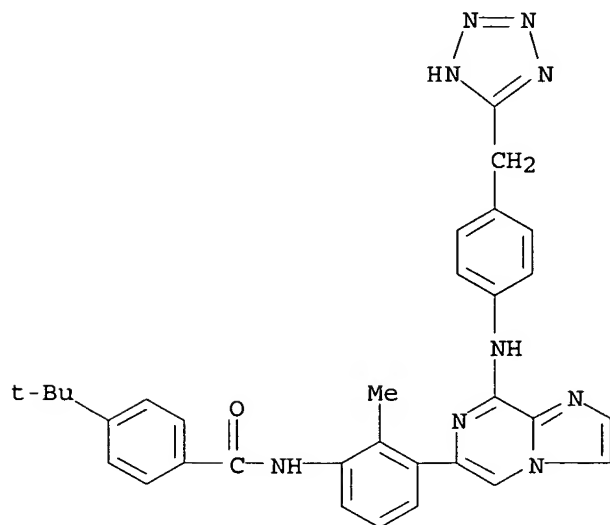


RN 886855-36-3 CAPLUS

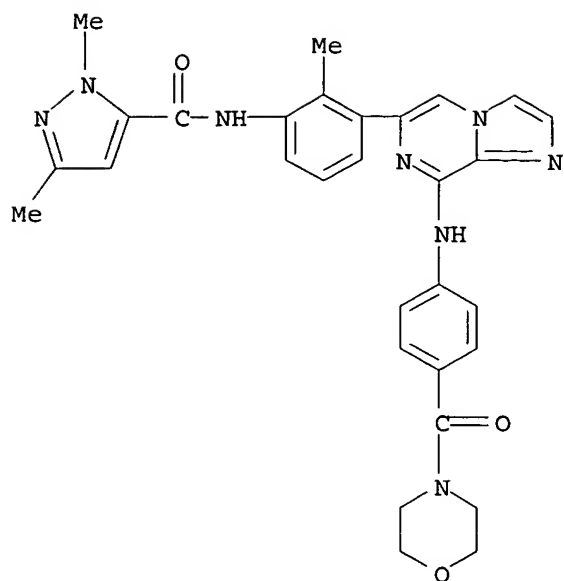
CN 3-Pyridinecarboxamide, 1,2-dihydro-6-methyl-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-2-oxo- (9CI) (CA INDEX NAME)



RN 886855-37-4 CAPLUS
 CN INDEX NAME NOT YET ASSIGNED

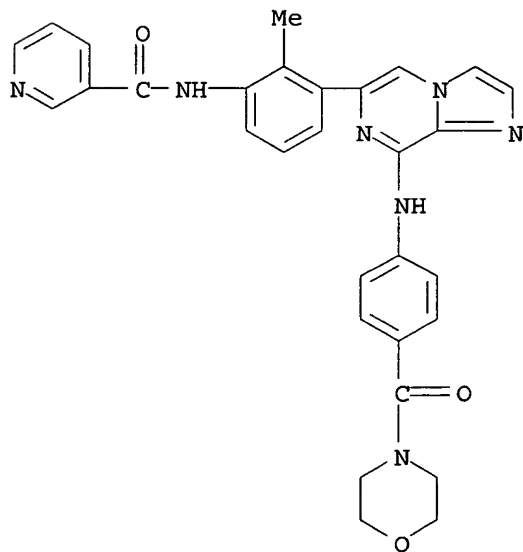


RN 886855-38-5 CAPLUS
 CN 1H-Pyrazole-5-carboxamide, 1,3-dimethyl-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
 (CA INDEX NAME)



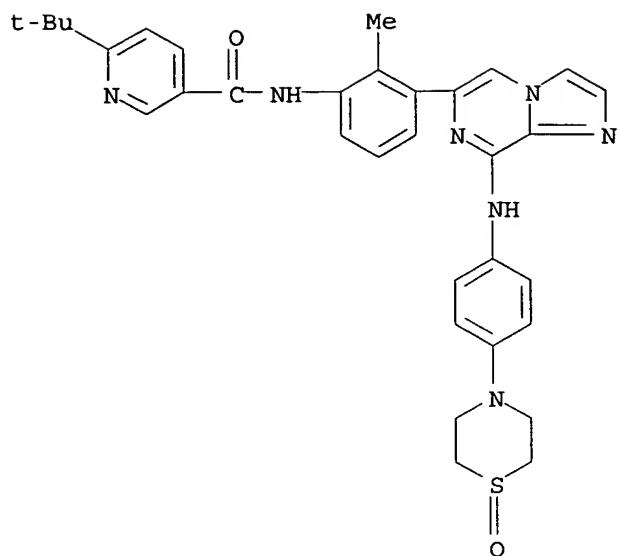
RN 886855-39-6 CAPLUS

CN 3-Pyridinecarboxamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



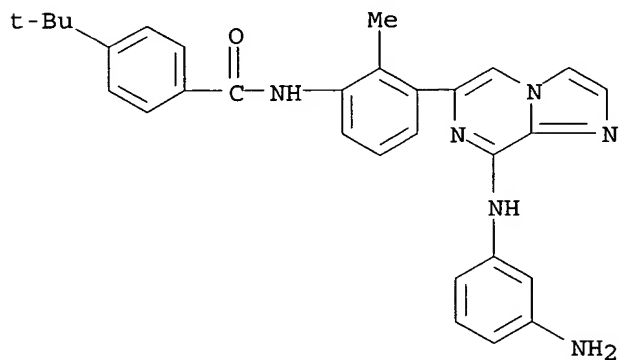
RN 886855-40-9 CAPLUS

CN 3-Pyridinecarboxamide, 6-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-(1-oxido-4-thiomorpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



RN 886855-41-0 CAPLUS

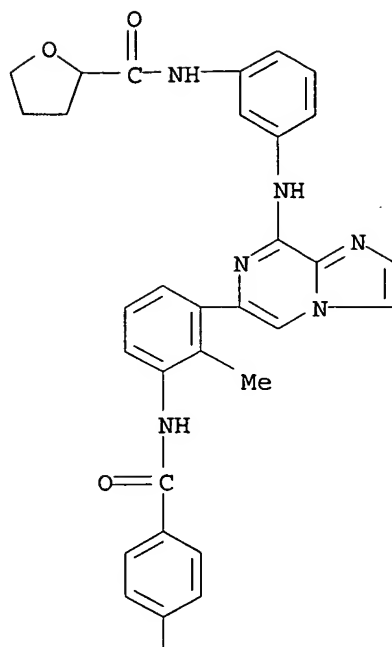
CN Benzamide, N-[3-[8-[(3-aminophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



RN 886855-42-1 CAPLUS

CN 2-Furancarboxamide, N-[3-[6-[3-[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]tetrahydro- (9CI) (CA INDEX NAME)

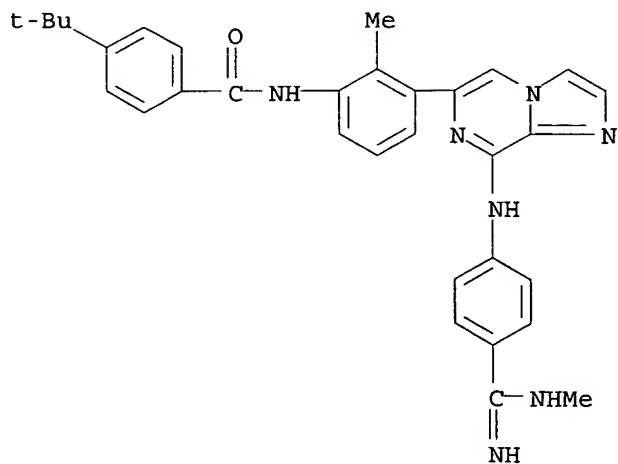
PAGE 1-A



PAGE 2-A

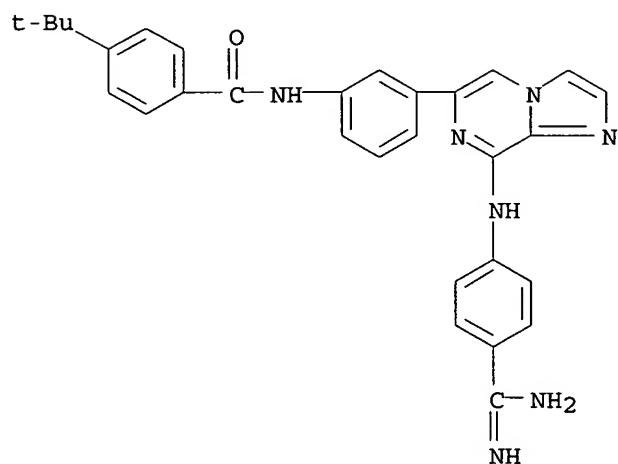


RN 886855-43-2 CAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[imino(methylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]- (9CI) (CA INDEX NAME)



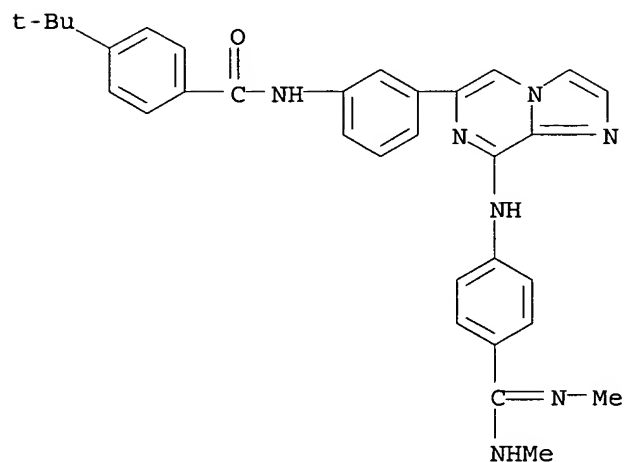
RN 886855-48-7 CAPLUS

CN Benzamide, N-[3-[8-[[4-(aminoiminomethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



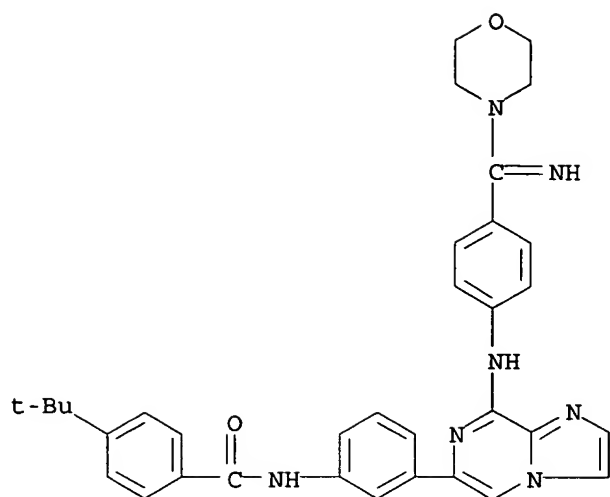
RN 886855-49-8 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(methylamino)(methylimino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



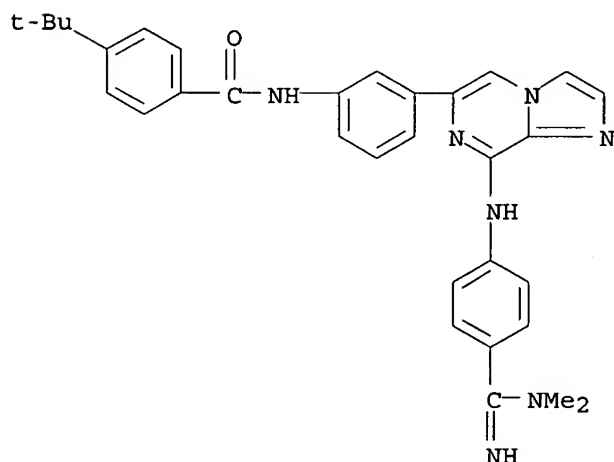
RN 886855-50-1 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(imino-4-morpholinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



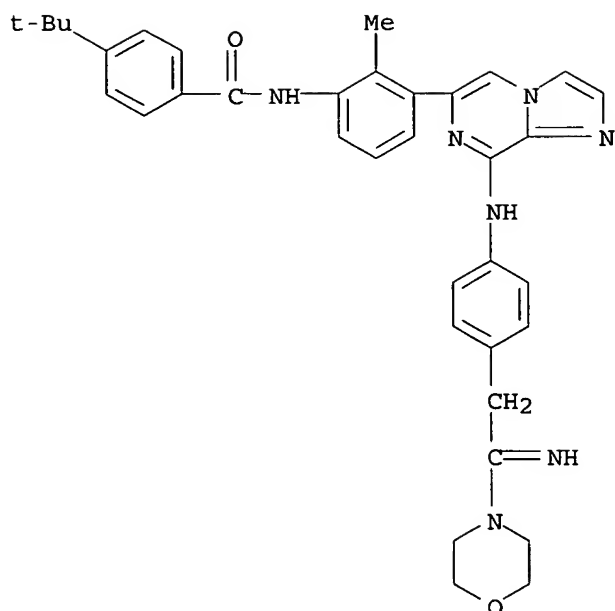
RN 886855-51-2 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(dimethylamino)iminomethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



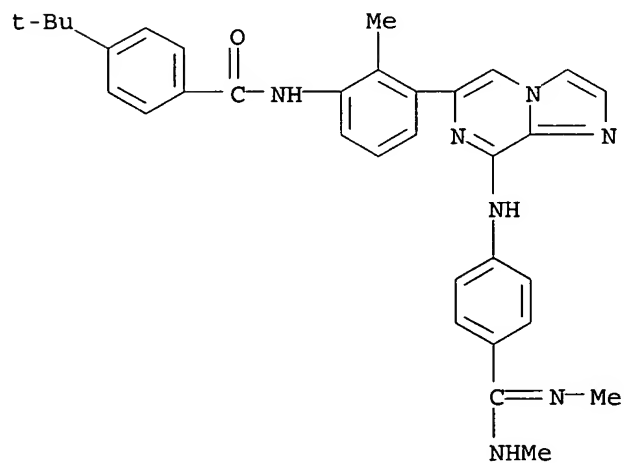
RN 886855-52-3 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-imino-2-(4-morpholinyl)ethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]- (9CI) (CA INDEX NAME)



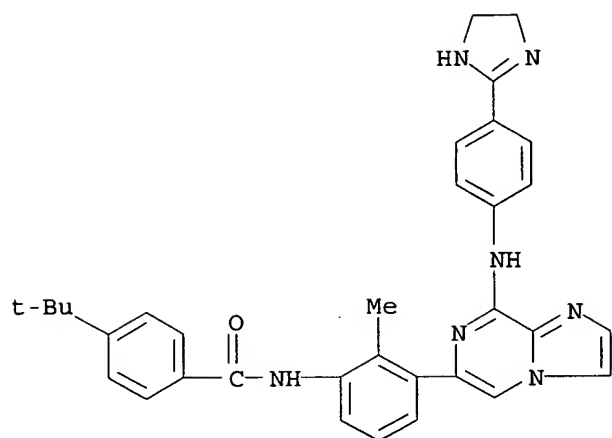
RN 886855-53-4 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-[(methylamino)(methylimino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



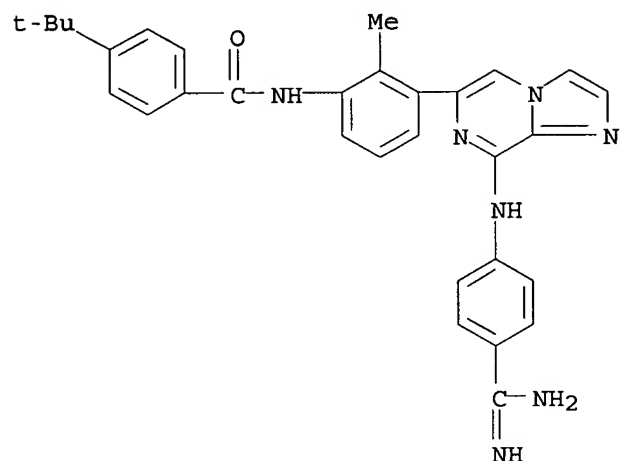
RN 886855-54-5 CAPLUS

CN Benzamide, N-[3-[8-[[4-(4,5-dihydro-1H-imidazol-2-yl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)-N-methyl-N-methylamino- (9CI) (CA INDEX NAME)



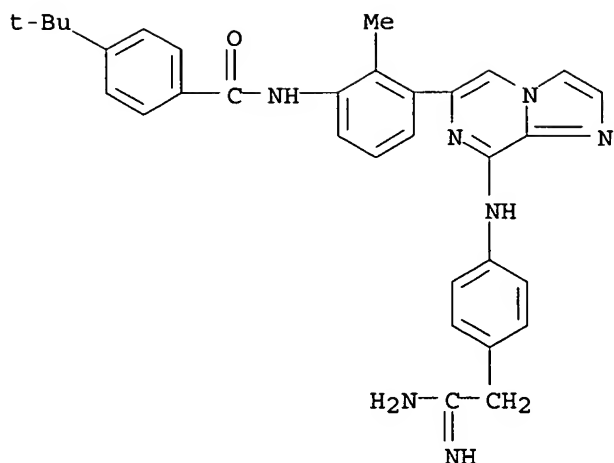
RN 886855-55-6 CAPLUS

CN Benzamide, N-[3-[8-[[4-(aminoiminomethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



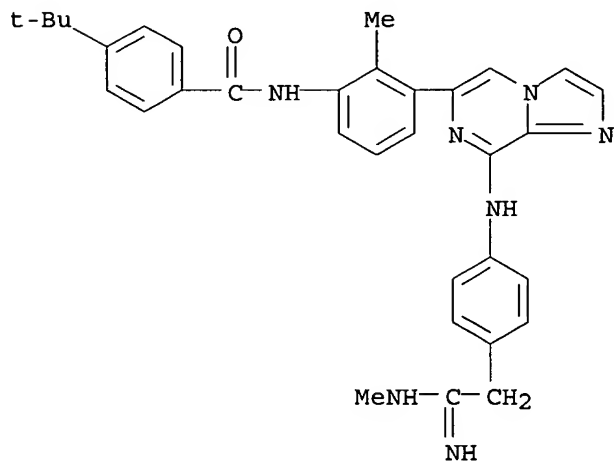
RN 886855-56-7 CAPLUS

CN Benzamide, N-[3-[8-[[4-(2-amino-2-iminoethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



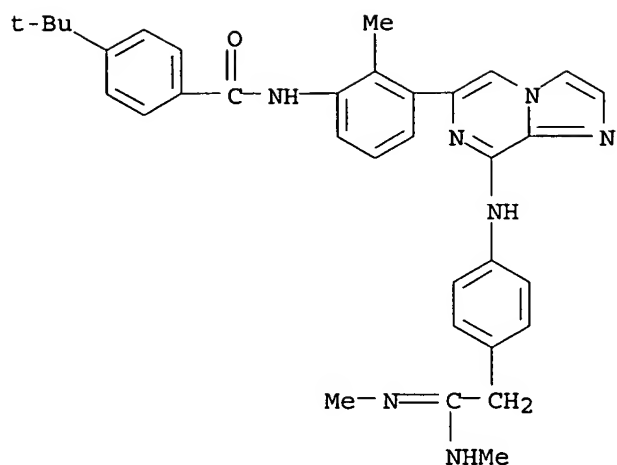
RN 886855-57-8 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-imino-2-(methylamino)ethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-(9CI) (CA INDEX NAME)



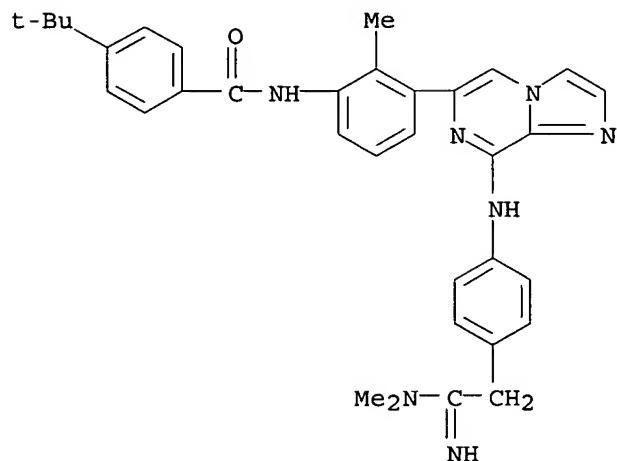
RN 886855-58-9 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[2-methyl-3-[8-[[4-[2-(methylamino)-2-(methylimino)ethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



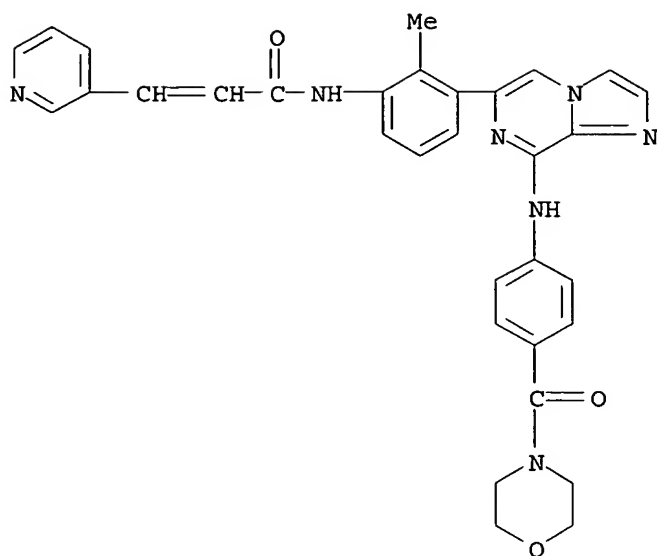
RN 886855-60-3 CAPLUS

CN Benzamide, N-[3-[8-[[4-[2-(dimethylamino)-2-iminoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



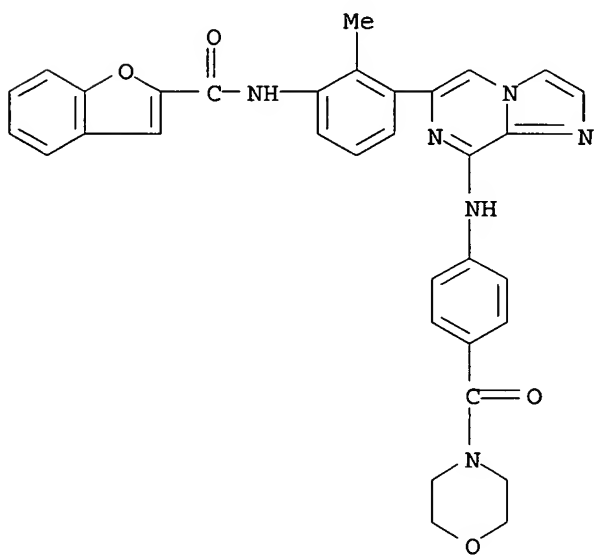
RN 886855-61-4 CAPLUS

CN 2-Propanamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-pyridinyl)- (9CI) (CA INDEX NAME)



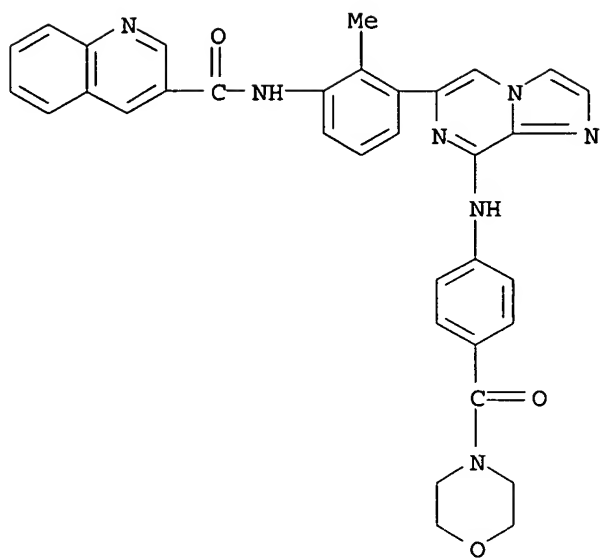
RN 886855-62-5 CAPLUS

CN 2-Benzofurancarboxamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



RN 886855-63-6 CAPLUS

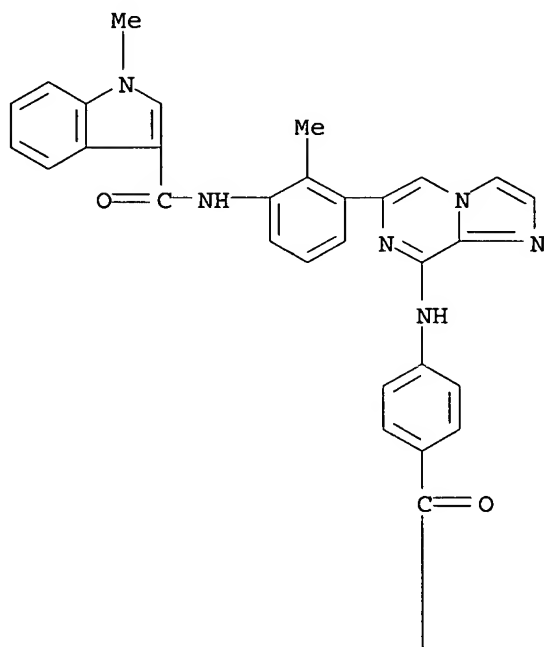
CN 3-Quinolinecarboxamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



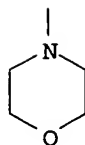
RN 886855-64-7 CAPLUS

CN 1H-Indole-3-carboxamide, 1-methyl-N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)

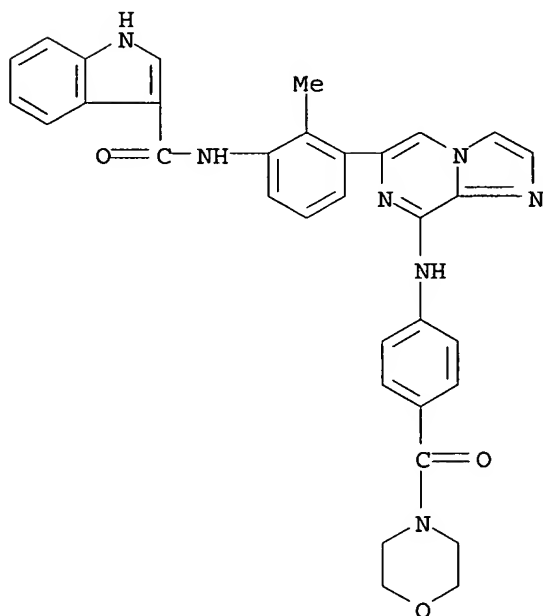
PAGE 1-A



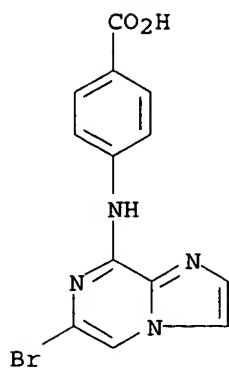
PAGE 2-A



RN 886855-65-8 CAPLUS
 CN 1H-Indole-3-carboxamide, N-[2-methyl-3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
 (CA INDEX NAME)

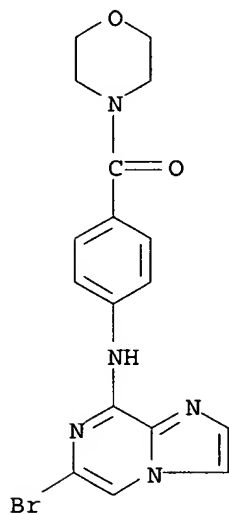


IT 886854-83-7P, 4-((6-Bromoimidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid 886854-84-8P, [4-((6-Bromoimidazo[1,2-a]pyrazin-8-yl)amino)phenyl] (morpholin-4-yl)methanone 886854-85-9P, [4-[[6-(3-Amino-2-methylphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl] (morpholin-4-yl)methanone 886854-86-0P, N-[6-(3-Amino-2-methylphenyl)imidazo[1,2-a]pyrazin-8-yl]-N-(4-((morpholin-4-yl)methyl)phenyl)amine 886855-44-3P, 4-((6-Bromoimidazo[1,2-a]pyrazin-8-yl)amino)benzonitrile 886855-45-4P, 4-[[6-(3-Amino-2-methylphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzonitrile 886855-46-5P, 4-tert-Butyl-N-[3-[8-((4-cyanophenyl)amino)imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]benzamide 886855-47-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of imidazopyrazinylamines as Btk kinase inhibitors)
 RN 886854-83-7 CAPLUS
 CN Benzoic acid, 4-[[6-bromoimidazo[1,2-a]pyrazin-8-yl]amino] - (9CI) (CA INDEX NAME)



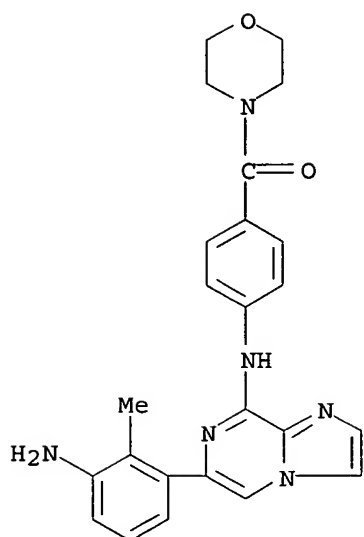
RN 886854-84-8 CAPLUS

CN Morpholine, 4-[4-[(6-bromoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl] - (9CI)
(CA INDEX NAME)



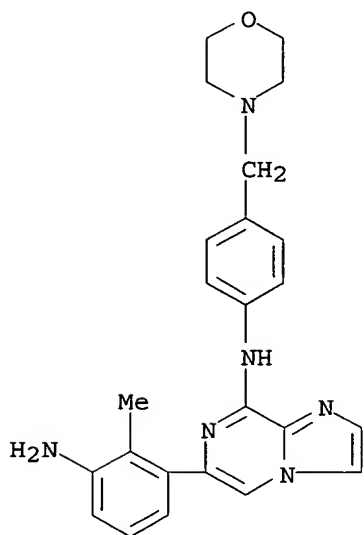
RN 886854-85-9 CAPLUS

CN Morpholine, 4-[4-[[6-(3-amino-2-methylphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl] - (9CI) (CA INDEX NAME)



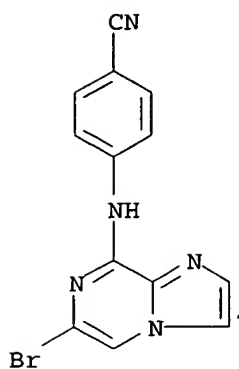
RN 886854-86-0 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-amino-2-methylphenyl)-N-[4-(4-morpholinylmethyl)phenyl]- (9CI) (CA INDEX NAME)



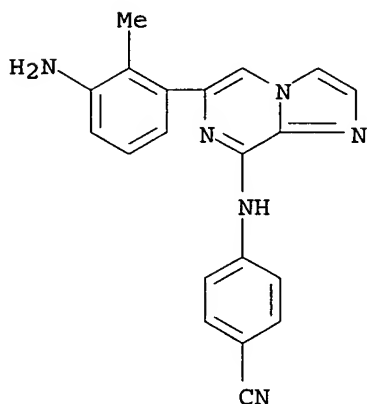
RN 886855-44-3 CAPLUS

CN Benzonitrile, 4-[(6-bromoimidazo[1,2-a]pyrazin-8-yl)amino]- (9CI) (CA INDEX NAME)



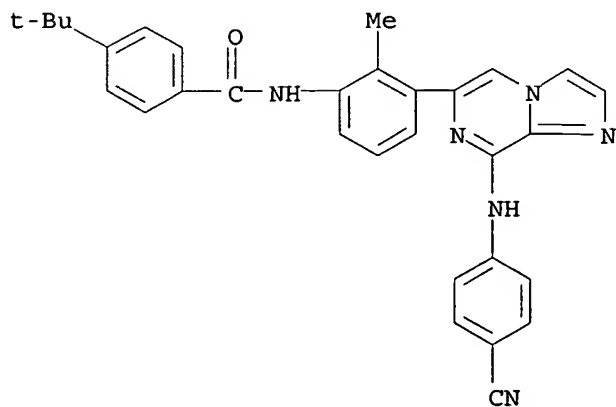
RN 886855-45-4 CAPLUS

CN Benzonitrile, 4-[[6-(3-amino-2-methylphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



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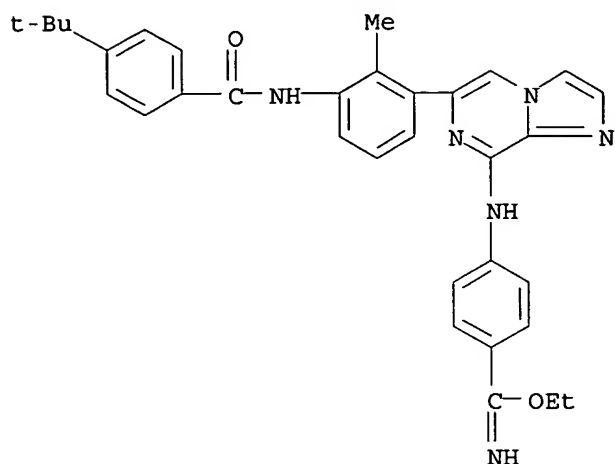
CN Benzamide, N-[3-[8-[(4-cyanophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



RN 886855-47-6 CAPLUS

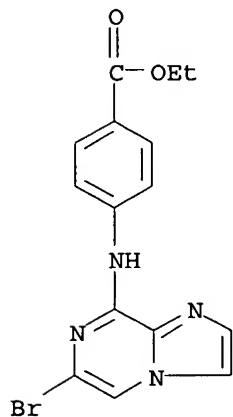
CN Benzenecarboximidic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-

methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester,
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

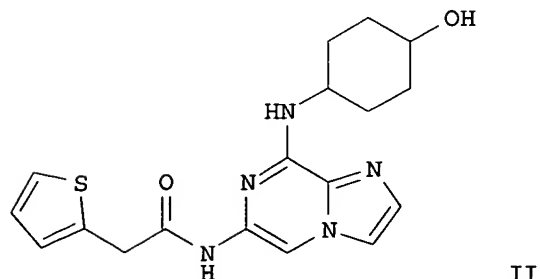
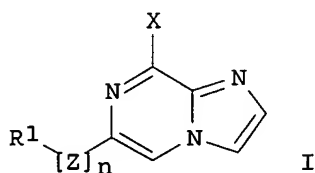
IT 886854-81-5, 4-((6-bromoimidazo[1,2-a]pyrazin-8-yl)amino)benzoic
acid ethyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of imidazopyrazinylamines as Btk kinase
inhibitors)
RN 886854-81-5 CAPLUS
CN Benzoic acid, 4-[(6-bromoimidazo[1,2-a]pyrazin-8-yl)amino]-, ethyl ester
(9CI) (CA INDEX NAME)



L38 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1004749 CAPLUS
DOCUMENT NUMBER: 143:306338
TITLE: Preparation of imidazo[1,2-a]pyrazine derivatives as
inhibitors of JNK kinases

INVENTOR(S) : Birault, Veronique; Harris, Clifford John; Harrison, Stephen Anthony
 PATENT ASSIGNEE(S) : Biofocus Discovery Limited, UK
 SOURCE : PCT Int. Appl., 63 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085252	A1	20050915	WO 2005-GB842	20050304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			GB 2004-4889	A 20040304
			GB 2004-26259	A 20041130
OTHER SOURCE(S) : MARPAT 143:306338				
ED Entered STN: 16 Sep 2005				
GI				



AB Title compds. I [R1 = (un)substituted heteroaryl, arylalkyl, aryl, etc.; X = NHR2, NR2R3 or OR2; R2 and R3 independently = H, (un)substituted heteroarylalkyl, heteroaryloxy, etc.; Z = NC(O), C(O)N, NS(O)2, etc.; n =

0-1] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of JNK kinases. Thus, e.g., II was prepared by coupling of 6,8-dibromo-imidazo[1,2-a]pyrazine (preparation given) with trans-4-aminocyclohexanol hydrochloride and subsequent amidation with thiophene-2-acetamide. The activity of I was evaluated in JNK screening assays and it was revealed that selected compds. of the invention displayed IC₅₀ values in the range of less than 1 μ M up to 10 μ M. I as inhibitor of JNK kinases should prove useful in the treatment of diseases such as but not limited to rheumatoid arthritis, multiple sclerosis and asthma. Pharmaceutical compns. comprising I are disclosed.

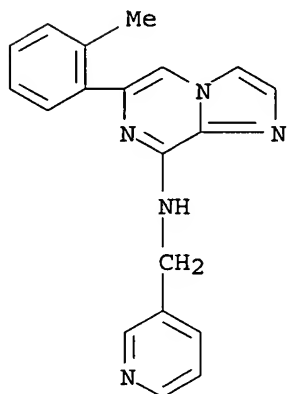
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 864545-99-3P 864546-00-9P 864546-01-0P
 864546-02-1P 864546-03-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazo[1,2-a]pyrazine derivs. as inhibitors of JNK kinases)

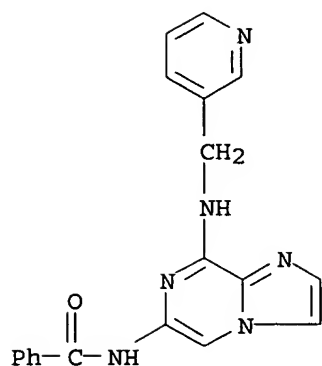
RN 864545-58-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-methylphenyl)-N-(3-pyridinylmethyl)-
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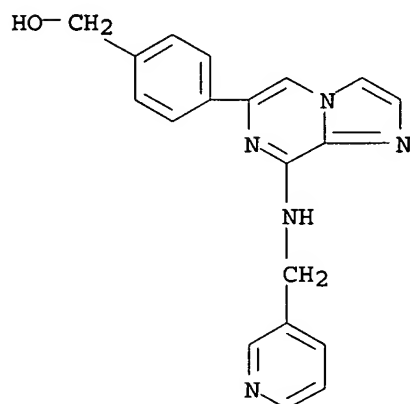
RN 864545-59-5 CAPLUS

CN Benzamide, N-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]-
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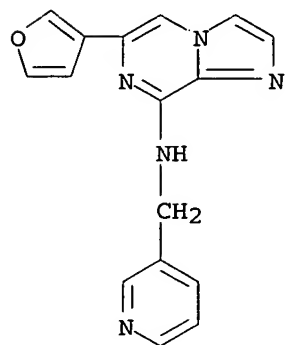
RN 864545-60-8 CAPLUS

CN Benzenemethanol, 4-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



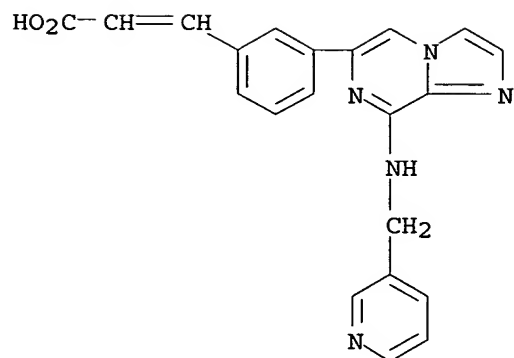
RN 864545-61-9 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-furanyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



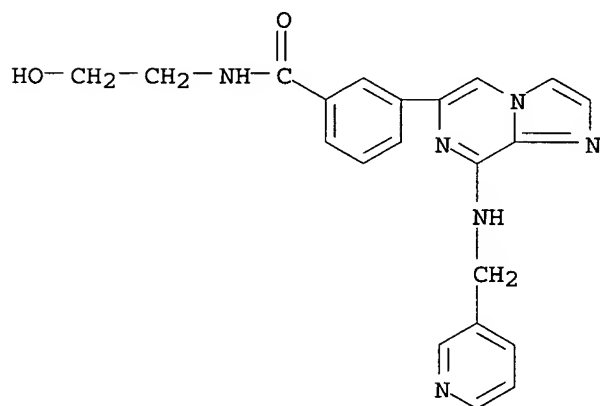
RN 864545-62-0 CAPLUS

CN 2-Propenoic acid, 3-[3-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



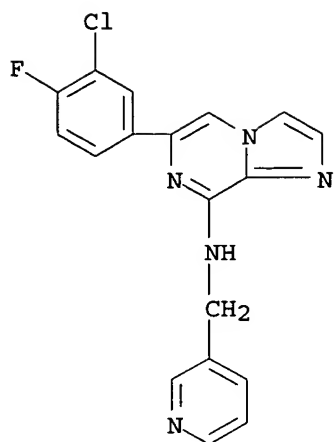
RN 864545-64-2 CAPLUS

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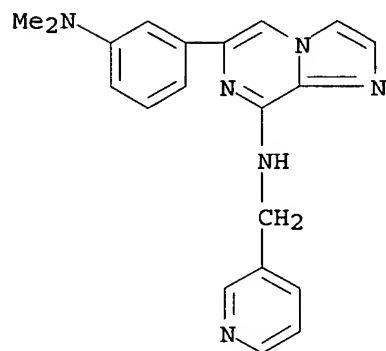
RN 864545-65-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-chloro-4-fluorophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



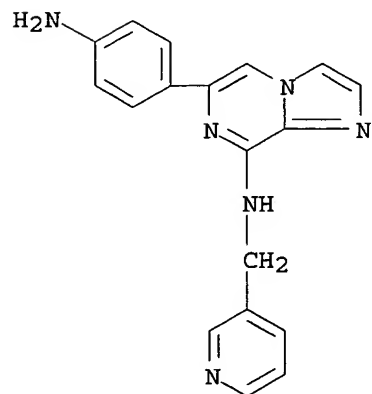
RN 864545-66-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3-(dimethylamino)phenyl]-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

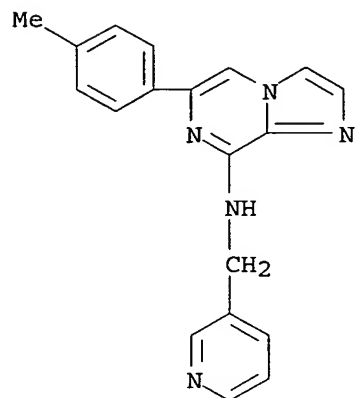


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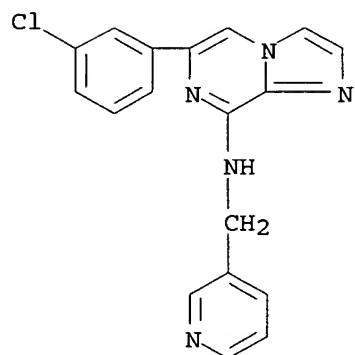
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(4-aminophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 864545-68-6 CAPLUS

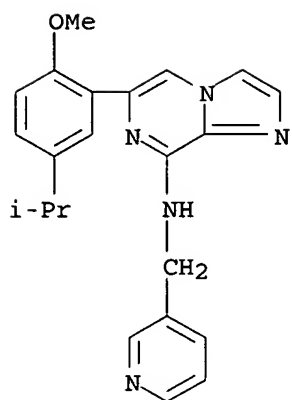
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(4-methylphenyl)-N-(3-pyridinylmethyl)-
(9CI) (CA INDEX NAME)

RN 864545-69-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-chlorophenyl)-N-(3-pyridinylmethyl)-
(9CI) (CA INDEX NAME)

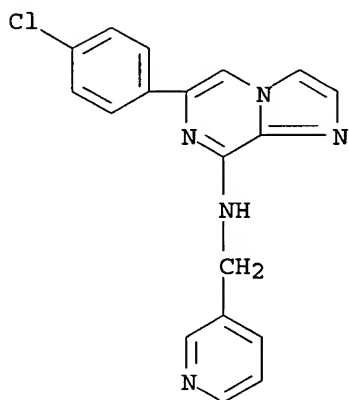
RN 864545-70-0 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[2-methoxy-5-(1-methylethyl)phenyl]-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



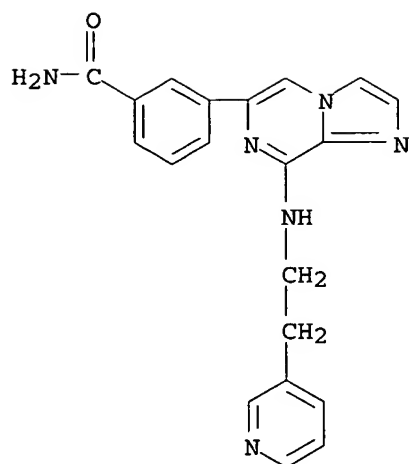
RN 864545-71-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(4-chlorophenyl)-N-(3-pyridinylmethyl)-
(9CI) (CA INDEX NAME)



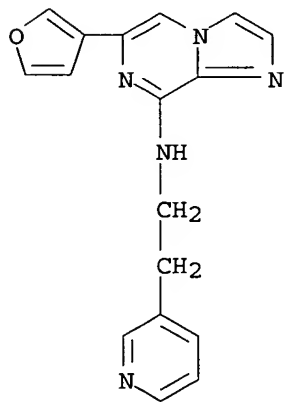
RN 864545-72-2 CAPLUS

CN Benzamide, 3-[8-[[2-(3-pyridinyl)ethyl]amino]imidazo[1,2-a]pyrazin-6-yl]-
(9CI) (CA INDEX NAME)



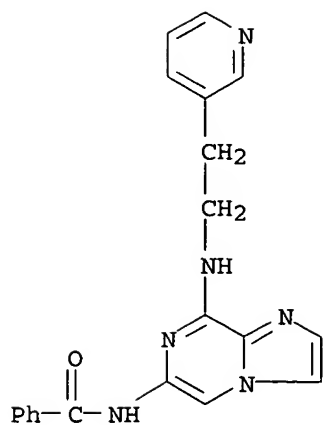
RN 864545-73-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-furanyl)-N-[2-(3-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)



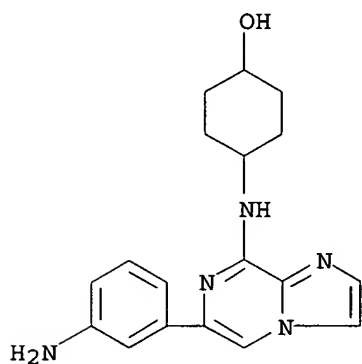
RN 864545-74-4 CAPLUS

CN Benzamide, N-[8-[[2-(3-pyridinyl)ethyl]amino]imidazo[1,2-a]pyrazin-6-yl]-
(9CI) (CA INDEX NAME)



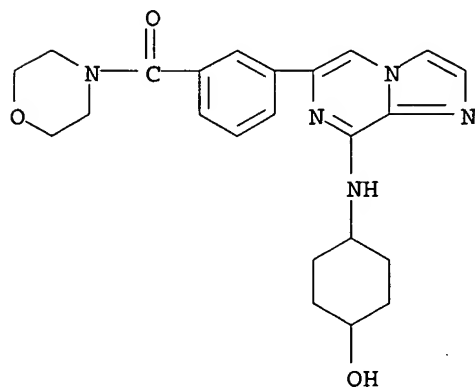
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CN Cyclohexanol, 4-[[6-(3-aminophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-(9CI) (CA INDEX NAME)



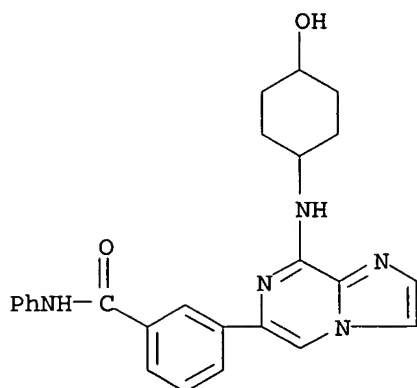
RN 864545-76-6 CAPLUS

CN Morpholine, 4-[3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]-(9CI) (CA INDEX NAME)



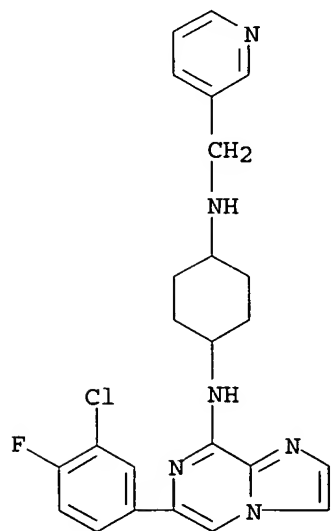
RN 864545-77-7 CAPLUS

CN Benamide, 3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-N-phenyl- (9CI) (CA INDEX NAME)



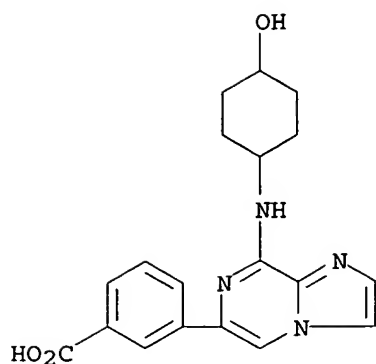
RN 864545-78-8 CAPLUS

CN 1,4-Cyclohexanediamine, N-[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



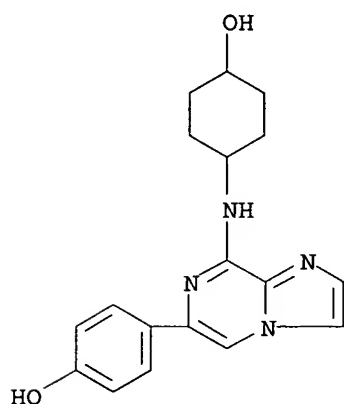
RN 864545-79-9 CAPLUS

CN Benzoic acid, 3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



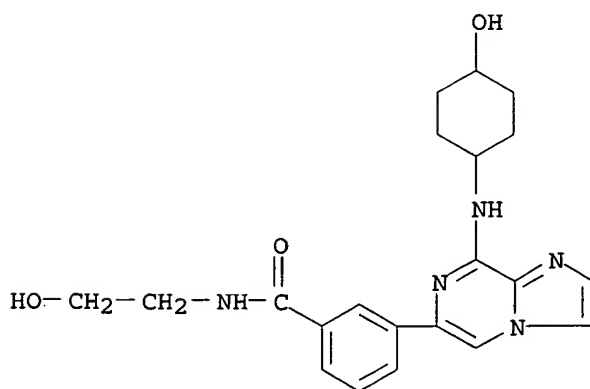
RN 864545-80-2 CAPLUS

CN Phenol, 4-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-(9CI) (CA INDEX NAME)



RN 864545-81-3 CAPLUS

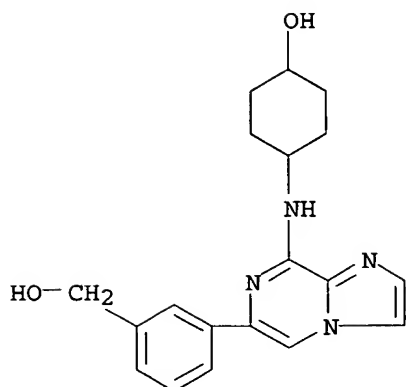
CN Benzamide, 3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-N-(2-hydroxyethyl)-(9CI) (CA INDEX NAME)



RN 864545-82-4 CAPLUS

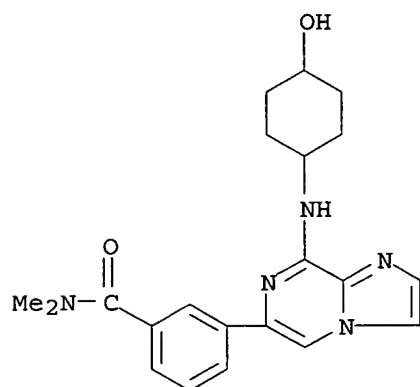
CN Benzenemethanol, 3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-

yl]- (9CI) (CA INDEX NAME)



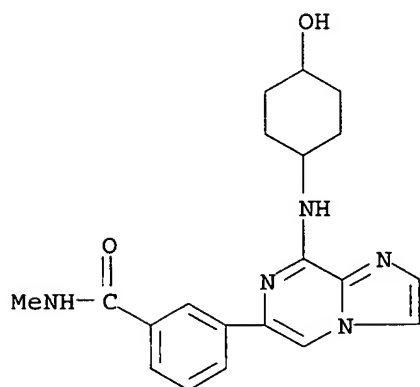
RN 864545-83-5 CAPLUS

CN Benzamide, 3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

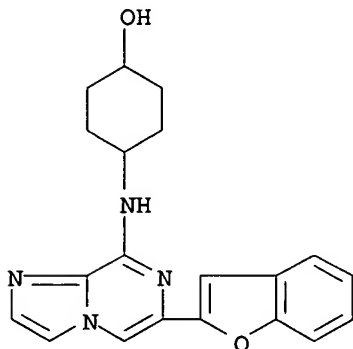


RN 864545-84-6 CAPLUS

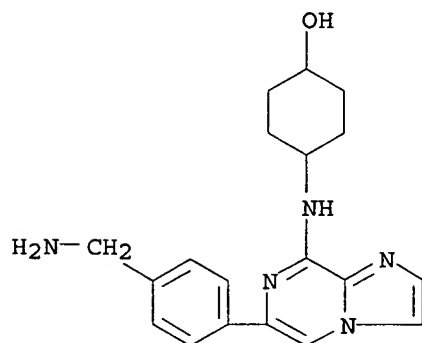
CN Benzamide, 3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-N-methyl- (9CI) (CA INDEX NAME)



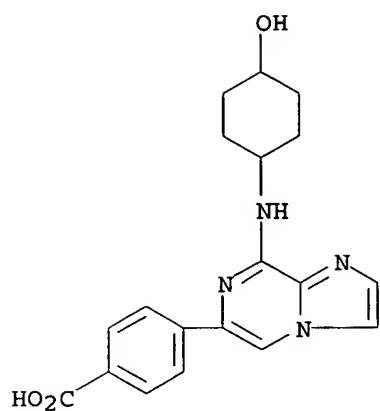
RN 864545-85-7 CAPLUS
CN Cyclohexanol, 4-[6-(2-benzofuranyl)imidazo[1,2-a]pyrazin-8-yl]amino] -
(9CI) (CA INDEX NAME)



RN 864545-86-8 CAPLUS
CN Cyclohexanol, 4-[6-[4-(aminomethyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino] - (9CI) (CA INDEX NAME)

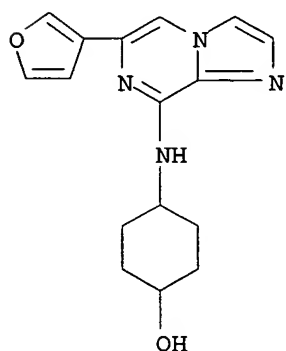


RN 864545-87-9 CAPLUS
CN Benzoic acid, 4-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl] -
(9CI) (CA INDEX NAME)



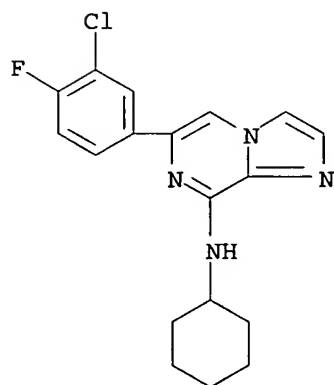
RN 864545-88-0 CAPLUS

CN Cyclohexanol, 4-[[6-(3-furanyl)imidazo[1,2-a]pyrazin-8-yl]amino] - (9CI)
(CA INDEX NAME)



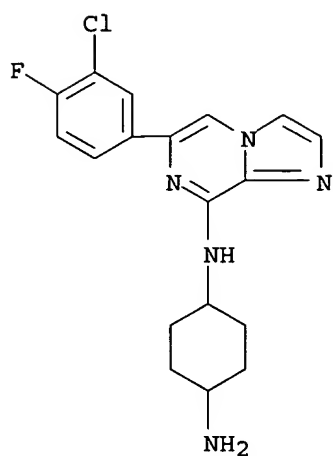
RN 864545-89-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-chloro-4-fluorophenyl)-N-cyclohexyl-
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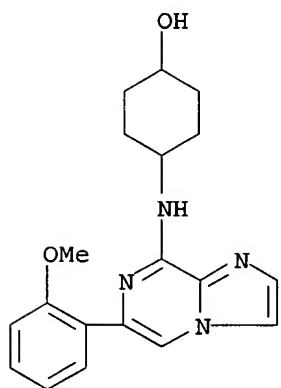
RN 864545-90-4 CAPLUS

CN 1,4-Cyclohexanediamine, N-[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]- (9CI) (CA INDEX NAME)



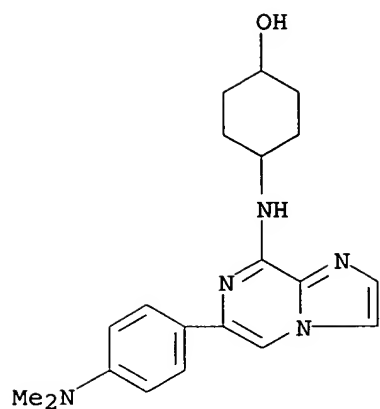
RN 864545-91-5 CAPLUS

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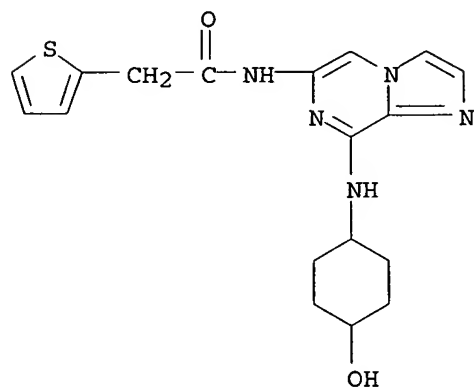
RN 864545-92-6 CAPLUS

CN Cyclohexanol, 4-[[6-[4-(dimethylamino)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



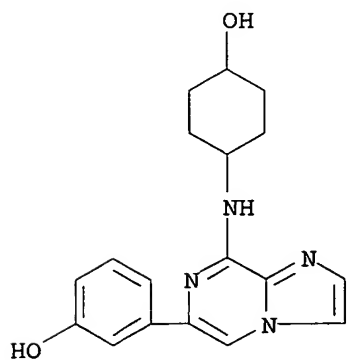
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CN 2-Thiopheneacetamide, N-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



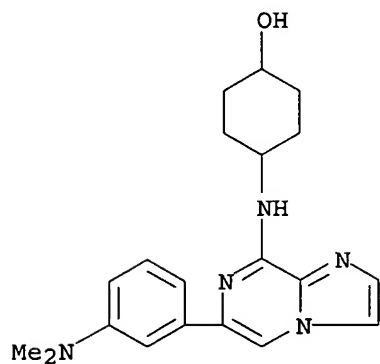
RN 864545-95-9 CAPLUS

CN Phenol, 3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



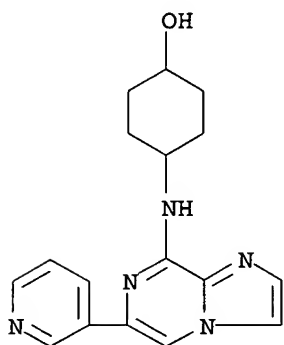
RN 864545-96-0 CAPLUS

CN Cyclohexanol, 4-[[6-[3-(dimethylamino)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



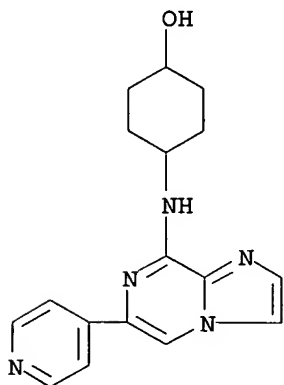
RN 864545-97-1 CAPLUS

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(CA INDEX NAME)



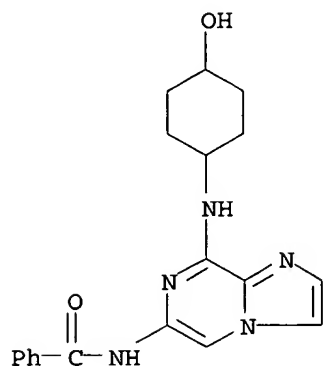
RN 864545-98-2 CAPLUS

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(CA INDEX NAME)



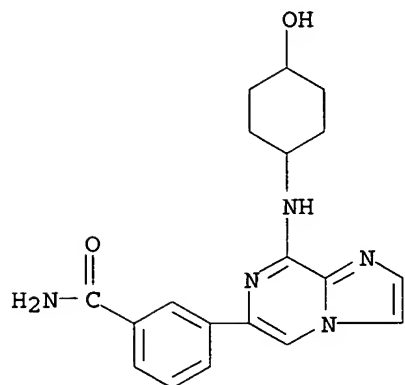
RN 864545-99-3 CAPLUS

CN Benzamide, N-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-(9CI) (CA INDEX NAME)



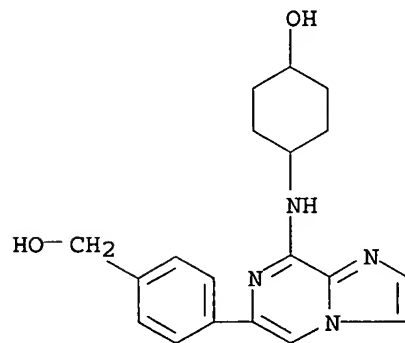
RN 864546-00-9 CAPLUS

CN Benzenemethanol, 4-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-(9CI) (CA INDEX NAME)



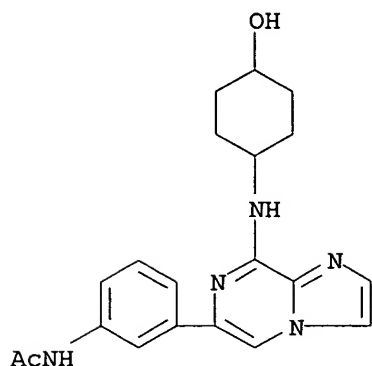
RN 864546-01-0 CAPLUS

CN Benzenemethanol, 4-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]-(9CI) (CA INDEX NAME)



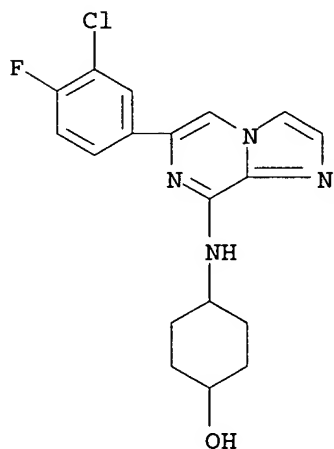
RN 864546-02-1 CAPLUS

CN Acetamide, N-[3-[8-[(4-hydroxycyclohexyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 864546-03-2 CAPLUS

CN Cyclohexanol, 4-[[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



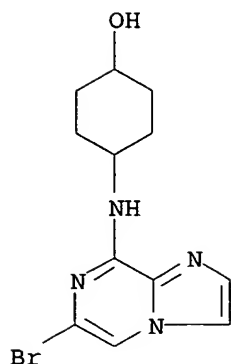
IT 864546-06-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of imidazo[1,2-a]pyrazine derivs. as inhibitors of JNK kinases)

RN 864546-06-5 CAPLUS

CN Cyclohexanol, 4-[(6-bromoimidazo[1,2-a]pyrazin-8-yl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:451386 CAPLUS

DOCUMENT NUMBER: 143:7734

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines as kinase modulators, particularly Btk inhibitors, for treating Btk-related diseases and conditions

INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Pippin, Douglas A.; Darrow, James W.; Mitchell, Scott A.

PATENT ASSIGNEE(S): Cellular Genomics Inc., USA

SOURCE: PCT Int. Appl., 236 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

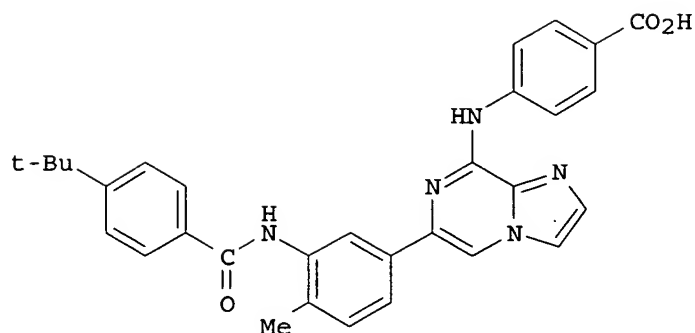
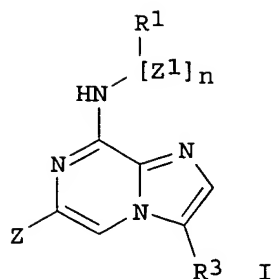
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005047290	A2	20050526	WO 2004-US37433	20041110
WO 2005047290	A3	20050811		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-519311P P 20031111

OTHER SOURCE(S): MARPAT 143:7734

ED Entered STN: 27 May 2005

GI



AB The title compds. [I; n = 0-1; Z1 = CO, CONH and derivs., NHSO2 and derivs., etc.; R1 = H, heterocyclo/cyclo/alkyl, alkoxy, (un)substituted Ph, heteroaryl, etc.; Z = -Z2-Q-R2; Z2 = (un)substituted phenylene, pyridylidene, naphthylidene; Q = CO, NHCO and derivs., CH2NH and derivs., SO2NH and derivs., etc.; R2 = (un)substituted heterocyclo/cyclo/alkyl, alkoxy, aryloxy, Ph, heteroaryl; R3 = H, cycloalkyl/heterocyclo/heterocycloalkylcyclo/alkyl] and their pharmaceutically acceptable salts, hydrates, solvates, crystal forms, diastereomers, and prodrugs, which are of particular utility in the treatment of Btk kinase-implicated disorders, were prepared. General methods of preparation were given. All exemplified compds. I such as II were tested in standard AKT-1 kinase assay and standard assay

to evaluate modulation of cell growth in soft agar (using cell lines HCT-15, MiaPaca2, MCF-7 and NIH3T3 clone stably overexpressing transfected myrAkt-1 human gene), and exhibited IC50 of $\leq 25 \mu\text{M}$. I were also tested in standard biochem. and cellular Btk and EphB4 assays; IC50 $< 1 \mu\text{M}$ in the biochem. assays. I and their formulations are useful for treating neoplasm, autoimmune and/or inflammatory conditions.

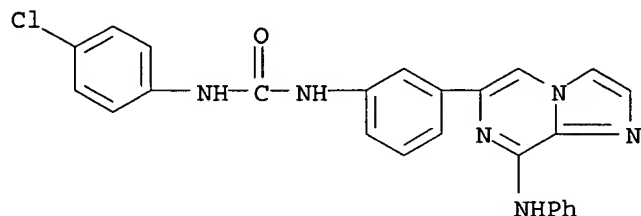
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 618455-88-2P 618455-91-7P 618455-94-0P
 618455-97-3P 618455-99-5P 852221-23-9P,
 4-[[6-[3-(4-tert-Butylbenzoylamino)-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid 852221-24-0P, 4-[[6-[3-(4-tert-Butylbenzoylamino)-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid 852221-25-1P, 4-[[6-[5-(4-tert-Butylbenzoylamino)-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid 852221-26-2P, 4-[[6-[3-(4-tert-Butylbenzoylamino)-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid ethyl ester

852221-27-3P, 4-tert-Butyl-N-[2-methyl-5-[8-(4-sulfamoylphenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazo[1,2-a]pyrazin-8-ylamines as kinase, particularly Btk, inhibitors)

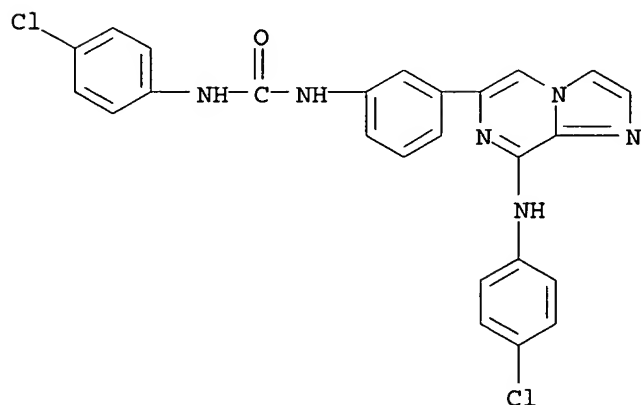
RN 618454-80-1 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



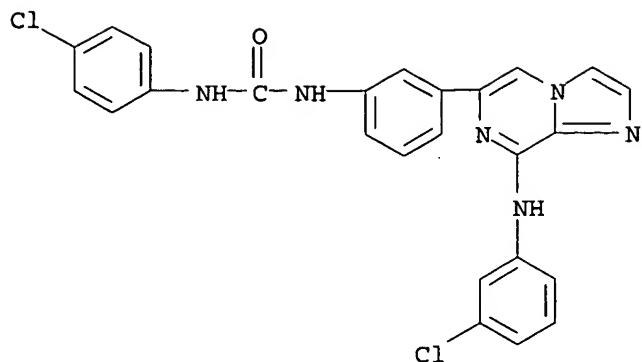
RN 618454-86-7 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



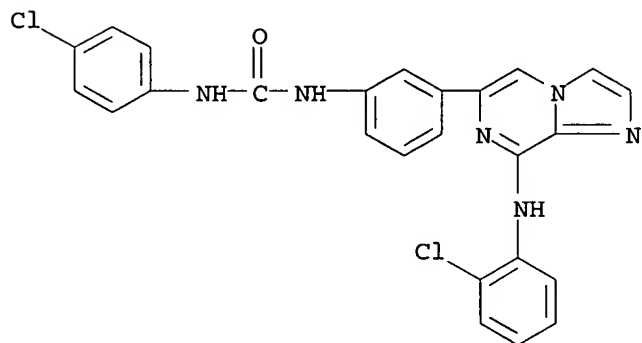
RN 618454-91-4 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



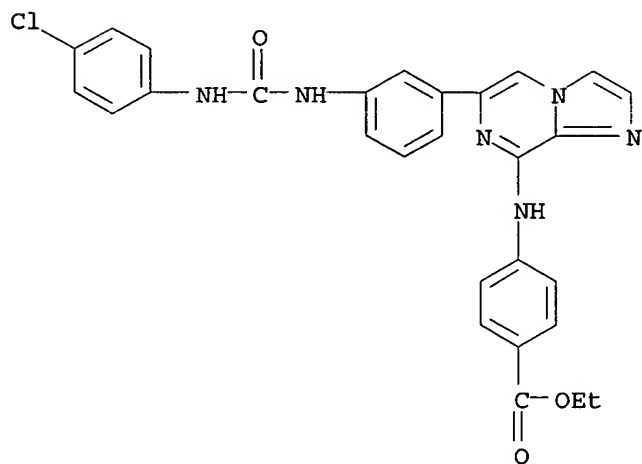
RN 618454-95-8 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 618455-30-4 CAPLUS

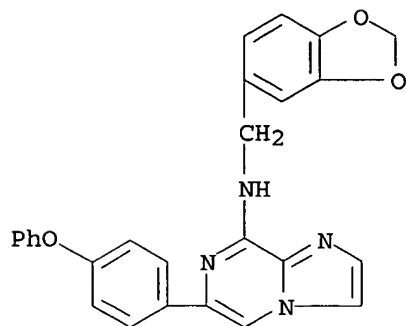
CN Benzoic acid, 4-[[6-[3-[[[(4-chlorophenyl)amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 618455-47-3 CAPLUS

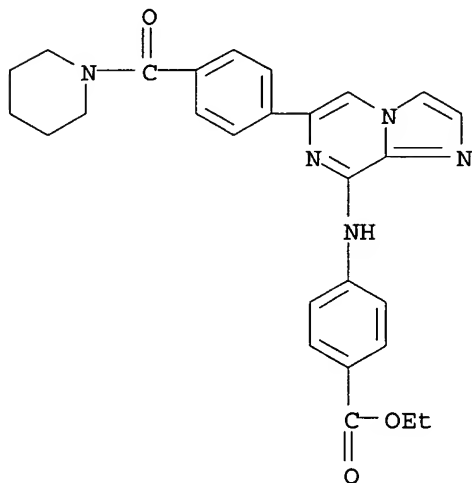
CN Imidazo[1,2-a]pyrazin-8-amine, N-(1,3-benzodioxol-5-ylmethyl)-6-(4-ethoxycarbonylphenyl)- (4-ethoxybenzoate salt)

phenoxyphenyl) - (9CI) (CA INDEX NAME)



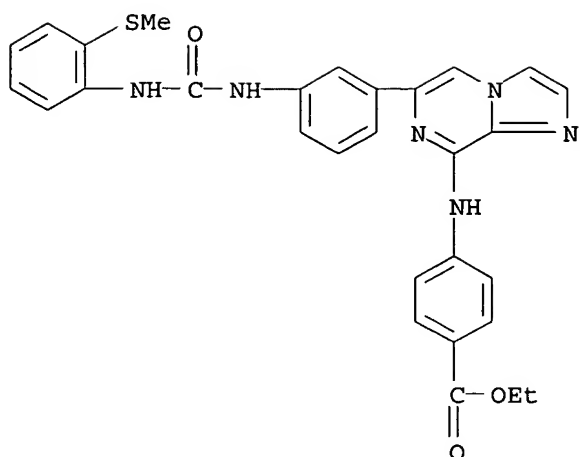
RN 618455-73-5 CAPLUS

CN Benzoic acid, 4-[[6-[[4-(1-piperidinylcarbonyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



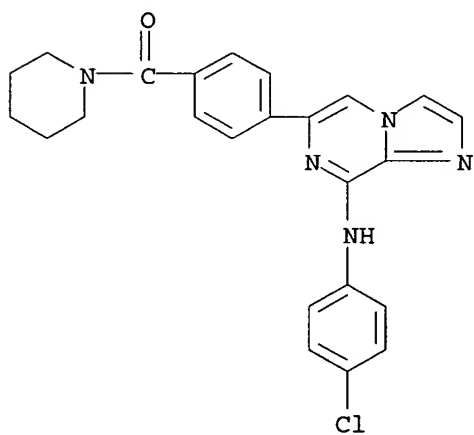
RN 618455-75-7 CAPLUS

CN Benzoic acid, 4-[[6-[[3-[[[2-(methylthio)phenyl]amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



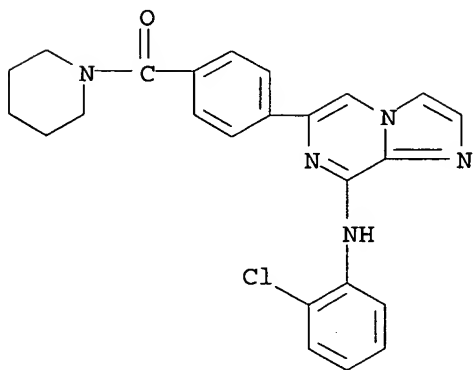
RN 618455-77-9 CAPLUS

CN Piperidine, 1-[4-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



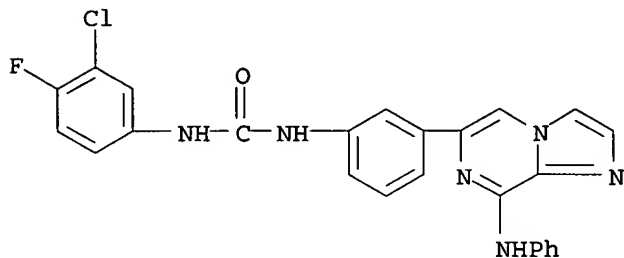
RN 618455-79-1 CAPLUS

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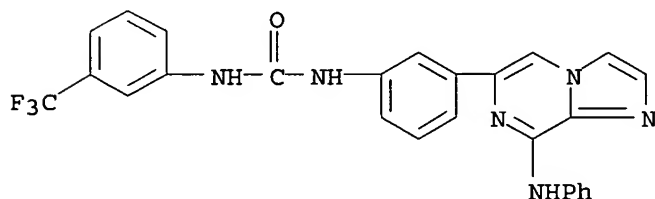
RN 618455-84-8 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



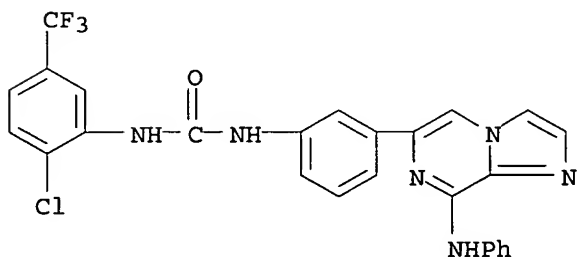
RN 618455-86-0 CAPLUS

CN Urea, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]-(9CI) (CA INDEX NAME)



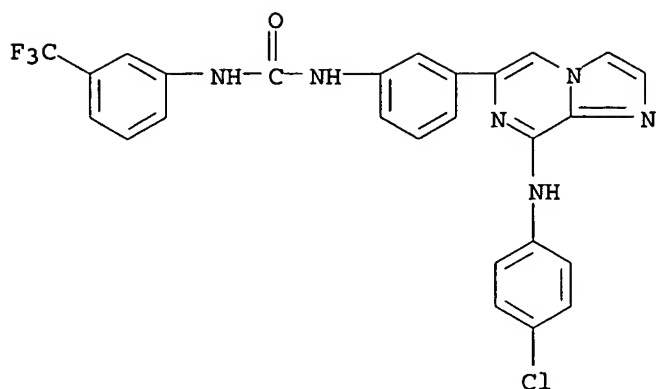
RN 618455-88-2 CAPLUS

CN Urea, N-[2-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



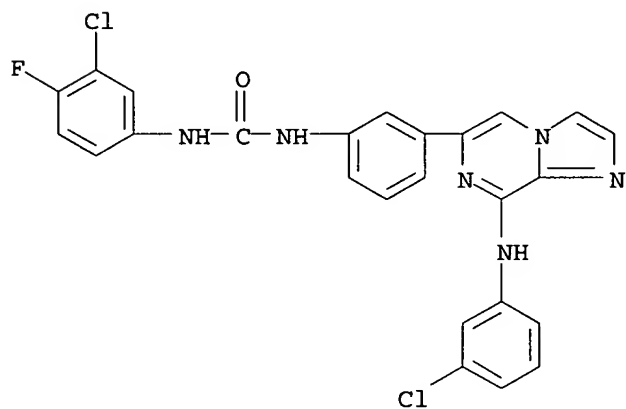
RN 618455-91-7 CAPLUS

CN Urea, N-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]-(9CI) (CA INDEX NAME)



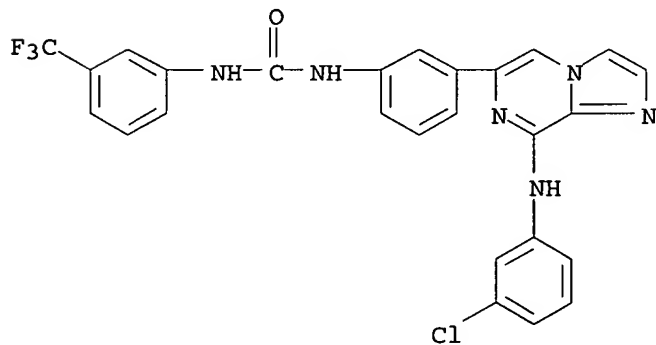
RN 618455-94-0 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 618455-97-3 CAPLUS

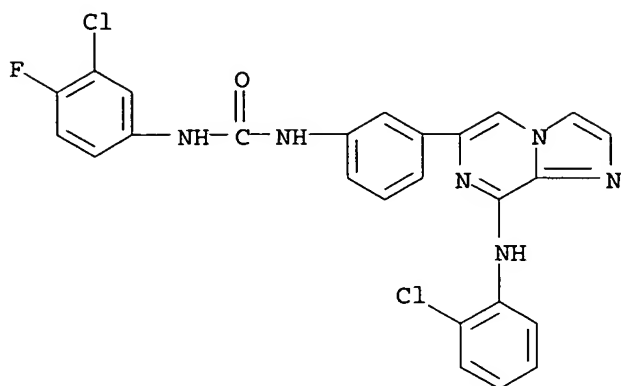
CN Urea, N-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 618455-99-5 CAPLUS

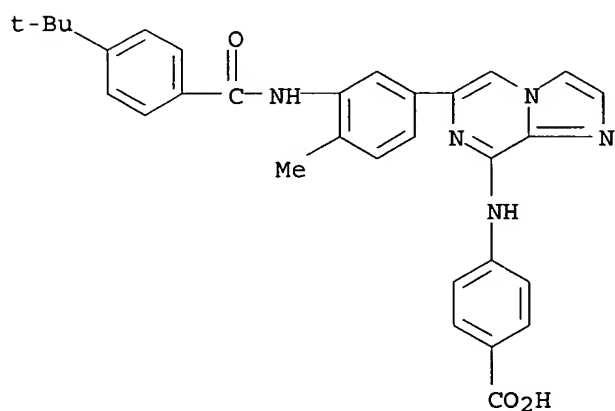
CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

chlorophenyl) amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



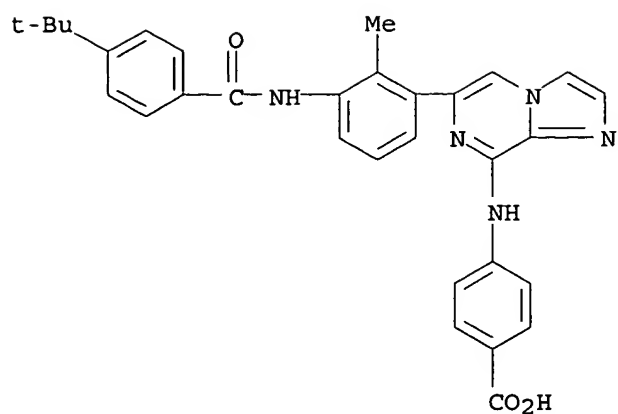
RN 852221-23-9 CAPLUS

CN Benzoic acid, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



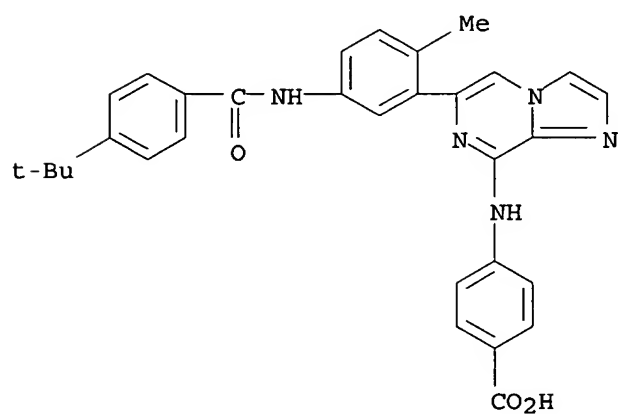
RN 852221-24-0 CAPLUS

CN Benzoic acid, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



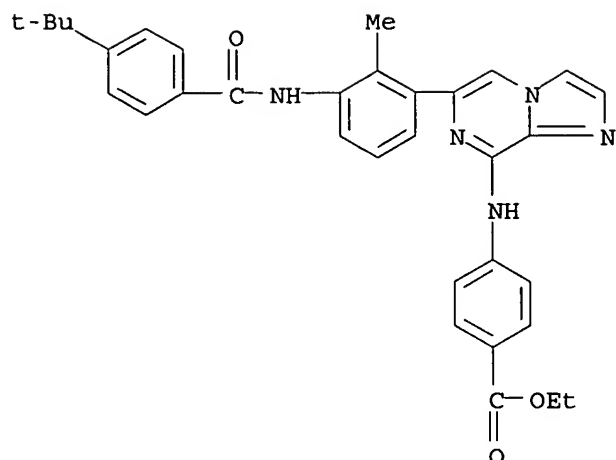
RN 852221-25-1 CAPLUS

CN Benzoic acid, 4-[[6-[5-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



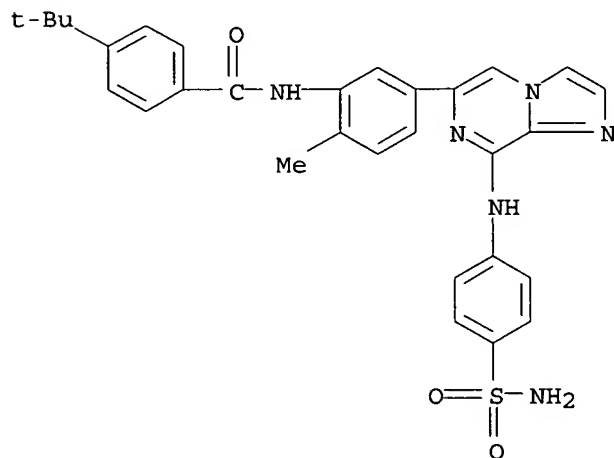
RN 852221-26-2 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-2-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 852221-27-3 CAPLUS

CN Benzamide, N-[5-[8-[[4-(aminosulfonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-2-methylphenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



L38 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:182665 CAPLUS

DOCUMENT NUMBER: 142:280228

TITLE: Preparation of imidazo[1,2-a]pyrazines as modulators of protein kinases, particularly EphB4 kinase

INVENTOR(S): Mitchell, Scott A.; Desimone, Robert W.; Darrow, James W.; Pippin, Douglas A.; Danca, M. Diana

PATENT ASSIGNEE(S): Cellular Genomics Inc., USA

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005019220 A2 20050303 WO 2004-US25884 20040811
 WO 2005019220 A3 20050324
 WO 2005019220 C2 20050602

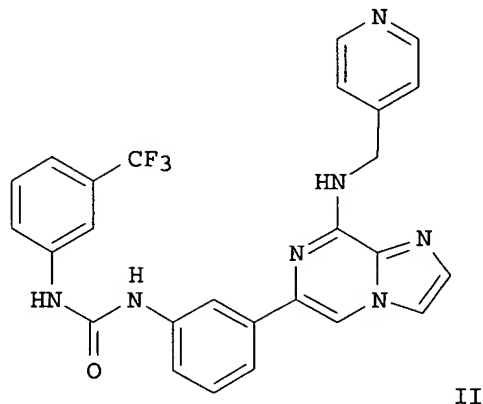
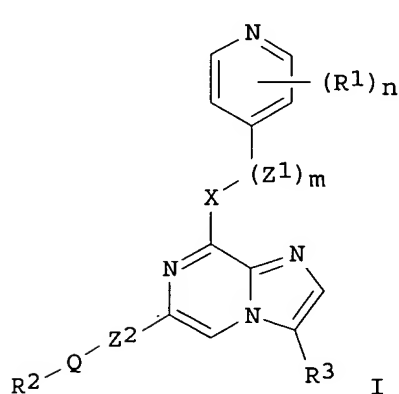
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 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

US 2005085484 A1 20050421 US 2004-915696 20040811
 PRIORITY APPLN. INFO.: US 2003-494179P P 20030811
 US 2004-540938P P 20040130
 US 2004-589738P P 20040721

OTHER SOURCE(S): MARPAT 142:280228

ED Entered STN: 04 Mar 2005

GI



AB Title compds. I [wherein n = 0-3; R¹ = hydroxy, nitro, cyano, amino or amido; R³ = H or (un)substituted (cyclo)alkyl; m = 1-4; Z¹ = CR⁴R⁵; R⁴, R⁵ = H, alkyl or halo; Z² = Ph; Q = (un)substituted ureido; X = O, S, CH₂ or (un)substituted amino; R² = (un)substituted alkyl or aryl; etc., or pharmaceutically acceptable salts thereof] were prepared as kinase modulators, particularly, as inhibitors of angiogenic and oncogenic kinases. For instance, urea II was synthesized in 4 steps: (1) deprotection of BrCH₂CH(OMe)₂ with HBr and cyclocondensation with 3,5-dibromo-2-aminopyrazine to give 6,8-dibromoimidazo[1,2-a]pyrazine; (2) aminolysis of the 8-bromo with 4-aminomethylpyridine; (3) Suzuki coupling of the 6-bromo with 3-H₂NC₆H₄B(OH)₂; and (4) carbamoylation of the amino group with 3-trifluoromethylphenyl isocyanate. In an assay for EphB4 kinase activity, using human recombinant EphB4 kinase cytoplasmic domain, compds. I had IC₅₀ values of 1 μM or less, with some particularly preferred compds. having values of 100 nM or less. Similar inhibitory potencies were found against PDGF-Rα, VEGF-R2, c-Kit, and Tie-2 kinases in vitro. Therefore, I and pharmaceutical compns. are useful for

treating diseases and disorders responsive to modulation of at least one of EphB4, PDGF-R α , VEGF-R2, c-Kit, and Tie-2 kinases, such as cancer.

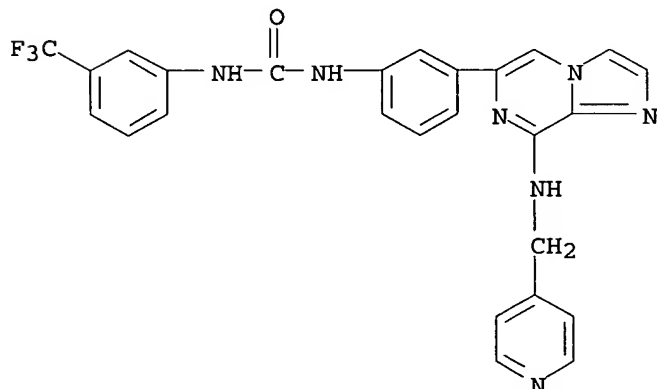
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847024-25-3P, 1-[3-[8-[(Pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(m-methylphenyl)urea 847024-26-4P,
1-(3-Chlorophenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-27-5P, 1-(4-Methyl-3-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-28-6P, 1-(5-Chloro-2-methoxyphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-29-7P, 1-(2-Chloro-5-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-33-3P, 1-[3-[8-[[2-(Pyridin-4-yl)ethyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea 847024-34-4P, 1-(5-Chloro-2-methoxyphenyl)-3-[3-[8-[[2-(pyridin-4-yl)ethyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-35-5P, 1-(2-Fluoro-5-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-36-6P, 1-(2-Methoxy-5-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-39-9P, 1-(5-Chloro-2,4-dimethoxyphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-40-2P, 1-[3-[8-[(Pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2,4,5-trichlorophenyl)urea 847024-43-5P, 1-(2-Methoxy-5-nitrophenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-44-6P, 1-(2-Ethoxy-5-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-45-7P, 1-(2-Isopropoxy-5-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-46-8P, 1-(2,4-Dimethoxy-5-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-48-0P, 1-(4-Ethoxy-3-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-49-1P, 1-(5-Chloro-2-phenoxyphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-50-4P, 1-(4-Fluoro-3-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-51-5P, 1-[2-(2-Methoxyethoxy)-5-trifluoromethylphenyl]-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-53-7P, 1-(2,4-Diethoxy-5-trifluoromethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-55-9P, 1-[2-(2-Hydroxyethoxy)-5-trifluoromethylphenyl]-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-56-0P, [[2-[3-[3-[8-[(Pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]ureido]-4-trifluoromethylphenyl]oxy]acetic acid 847024-57-1P, 1-[2-(2-Methylaminoethoxy)-5-trifluoromethylphenyl]-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-58-2P, 1-[2-(2-Dimethylaminoethoxy)-5-trifluoromethylphenyl]-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-59-3P, 1-(3-Chloro-4-hydroxymethylphenyl)-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-60-6P, 1-[5-Chloro-2-[[[1,3]dioxolan-2-yl)methoxy]phenyl]-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-61-7P, 1-[5-Chloro-2-(2-hydroxyethoxy)phenyl]-3-[3-[8-[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 847024-62-8P, 1-[5-Chloro-2-(2-methylaminoethoxy)phenyl]-3-[3-[8-

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 847024-66-2P, 1-[2-(3-Hydroxypropoxy)-5-trifluoromethylphenyl]-3-
 [3-[8-[[(pyridin-4-yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea
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 yl]phenyl]urea 847024-68-4P, 1-[5-Chloro-2-(3-
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 ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-[2-[2-(pyrrolidin-1-
 yl)ethoxy]-5-trifluoromethylphenyl]urea 847024-71-9P,
 1-(2-Hydroxy-5-trifluoromethylphenyl)-3-[3-[8-[[(pyridin-4-
 yl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(inhibitor; preparation of imidazopyrazines as kinase inhibitors)

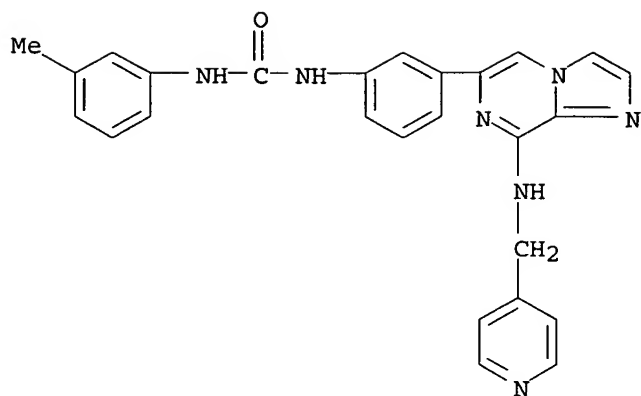
RN 673857-16-4 CAPLUS

CN Urea, N-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-
 N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



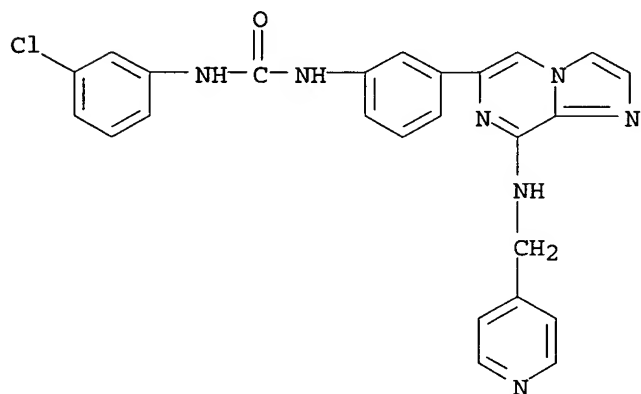
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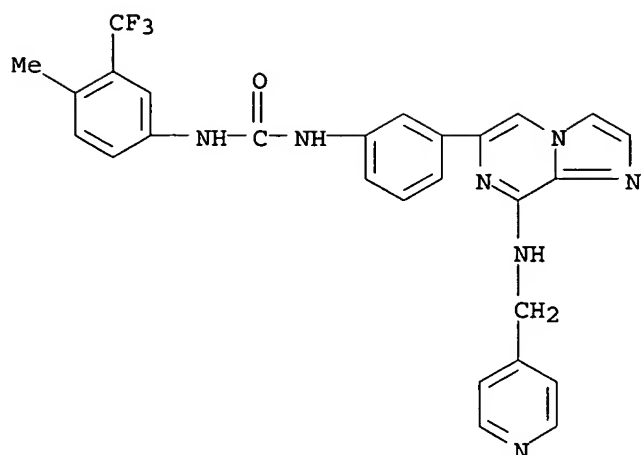
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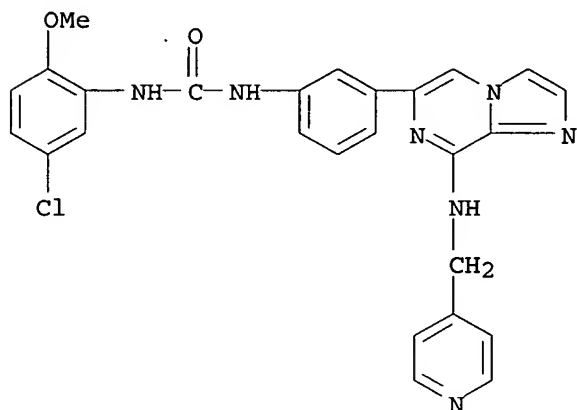
RN 847024-27-5 CAPLUS

CN Urea, N-[4-methyl-3-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



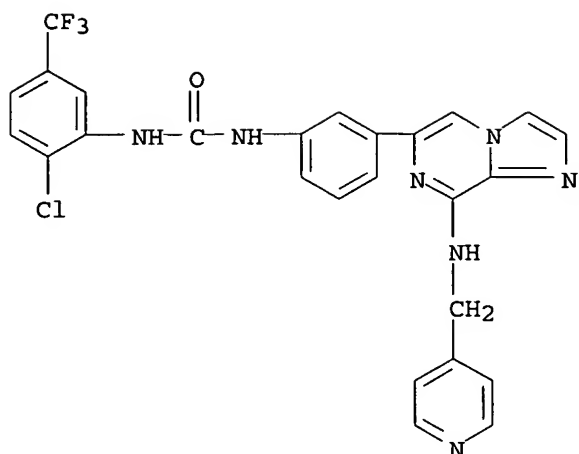
RN 847024-28-6 CAPLUS

CN Urea, N-(5-chloro-2-methoxyphenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



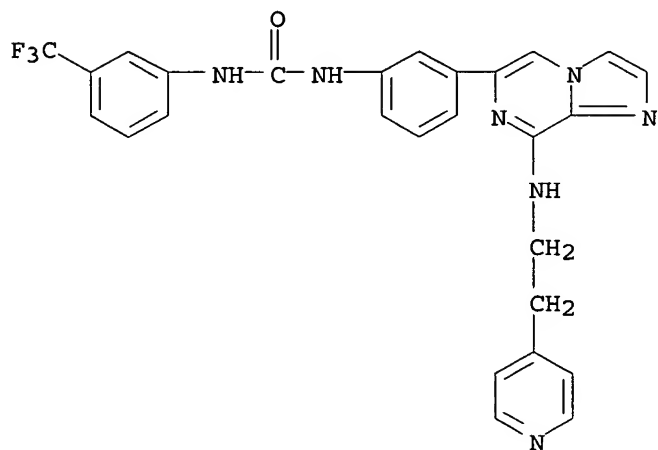
RN 847024-29-7 CAPLUS

CN Urea, N-[2-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



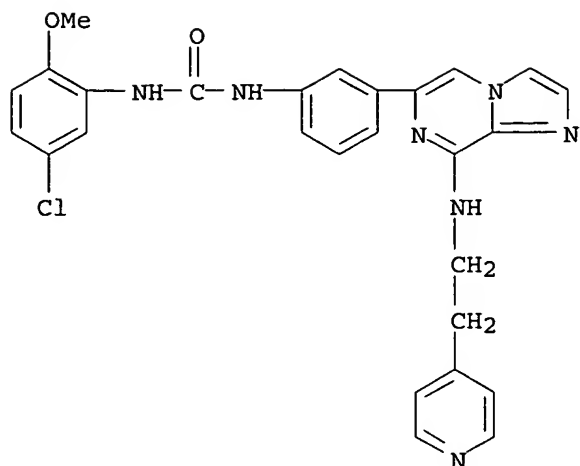
RN 847024-33-3 CAPLUS

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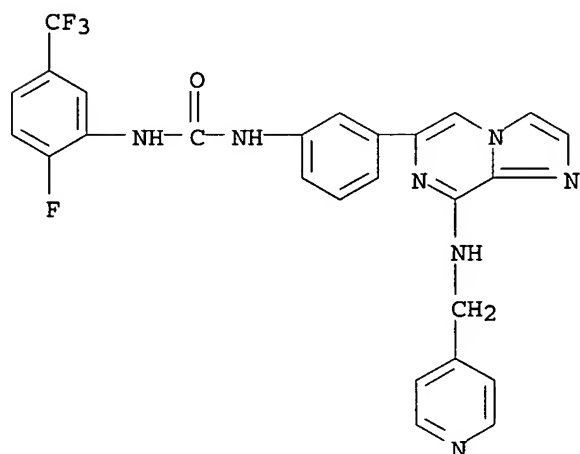
RN 847024-34-4 CAPLUS

CN Urea, N-(5-chloro-2-methoxyphenyl)-N'-[3-[8-[[2-(4-pyridinyl)ethyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



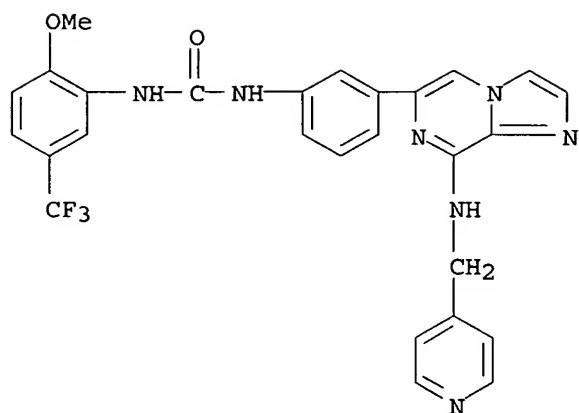
RN 847024-35-5 CAPLUS

CN Urea, N-[2-fluoro-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



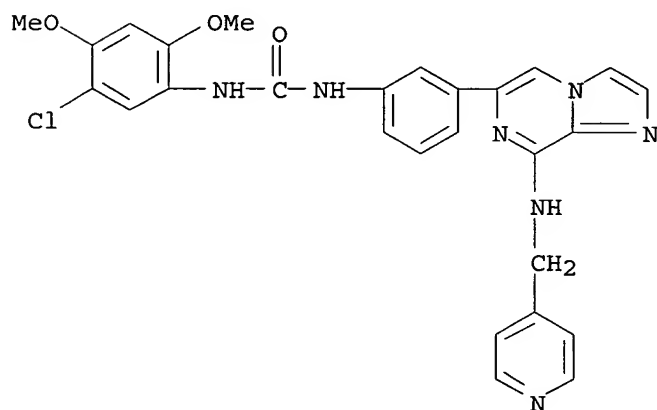
RN 847024-36-6 CAPLUS

CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



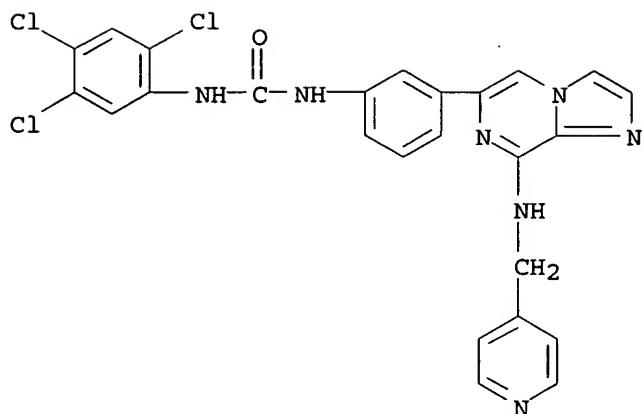
RN 847024-39-9 CAPLUS

CN Urea, N-(5-chloro-2,4-dimethoxyphenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



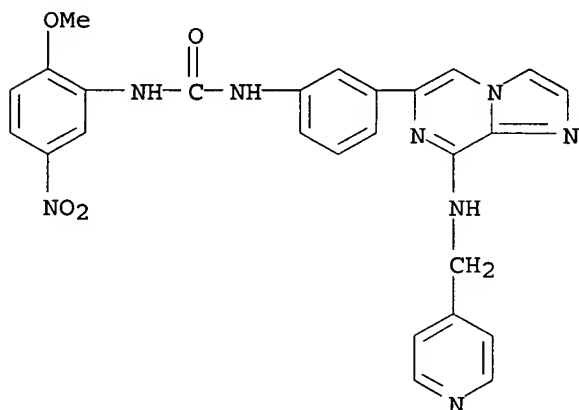
RN 847024-40-2 CAPLUS

CN Urea, N-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2,4,5-trichlorophenyl)- (9CI) (CA INDEX NAME)



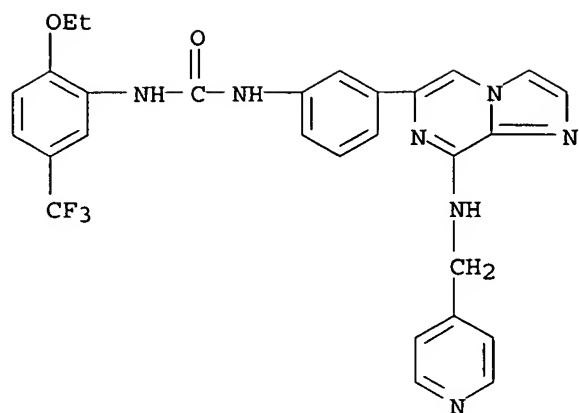
RN 847024-43-5 CAPLUS

CN Urea, N-(2-methoxy-5-nitrophenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



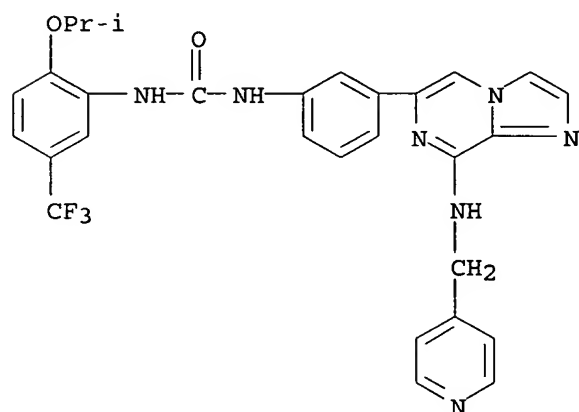
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CN Urea, N-[2-ethoxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



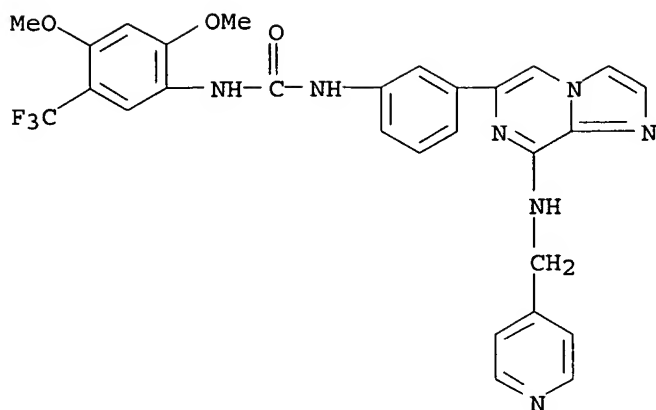
RN 847024-45-7 CAPLUS

CN Urea, N-[2-(1-methylethoxy)-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



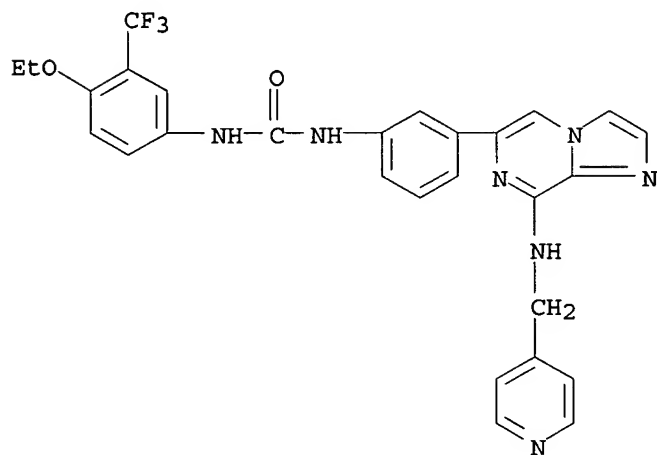
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CN Urea, N-[2,4-dimethoxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



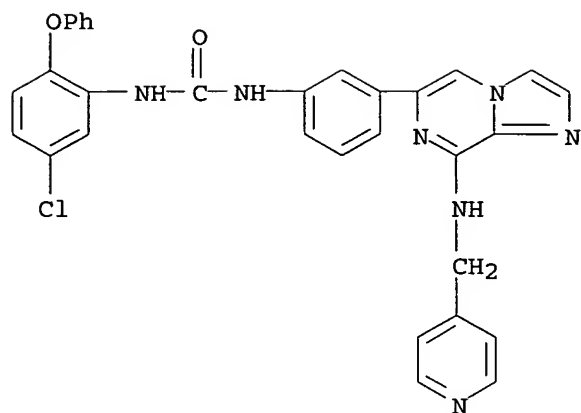
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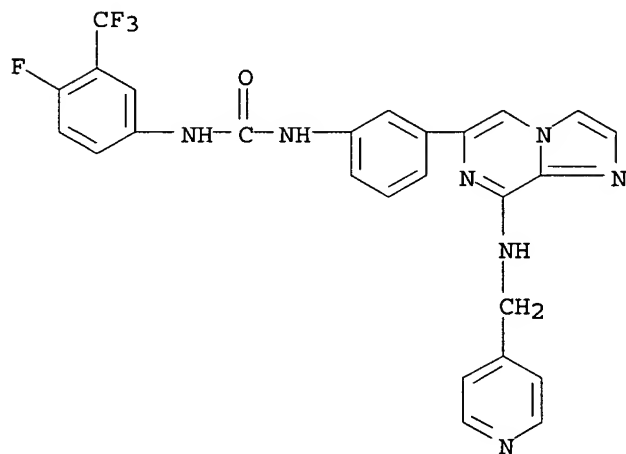
RN 847024-49-1 CAPLUS

CN Urea, N-(5-chloro-2-phenoxyphenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



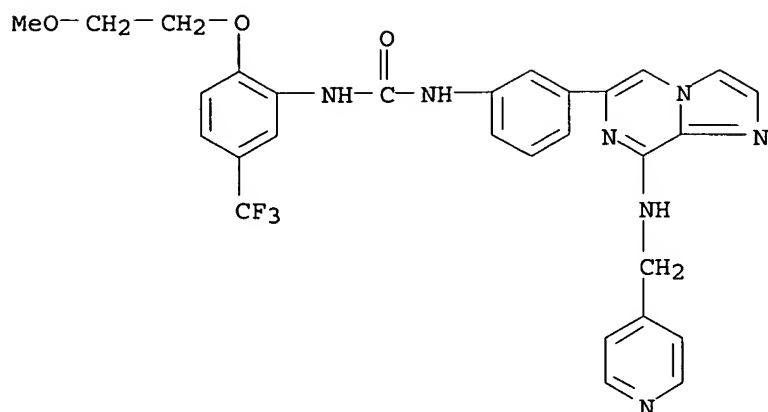
RN 847024-50-4 CAPLUS

CN Urea, N-[4-fluoro-3-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



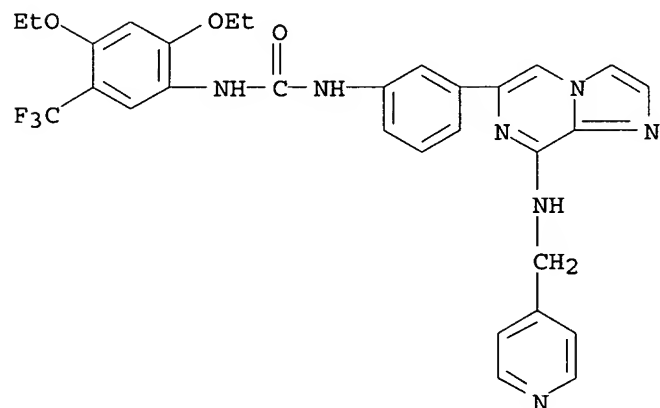
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CN Urea, N-[2-(2-methoxyethoxy)-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



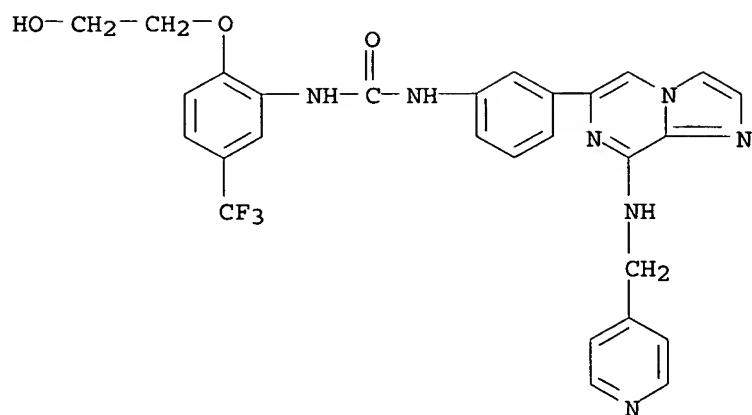
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CN Urea, N-[2,4-diethoxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



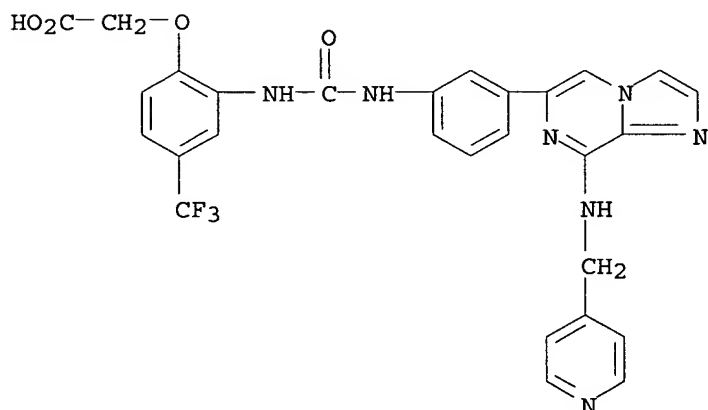
RN 847024-55-9 CAPLUS

CN Urea, N-[2-(2-hydroxyethoxy)-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



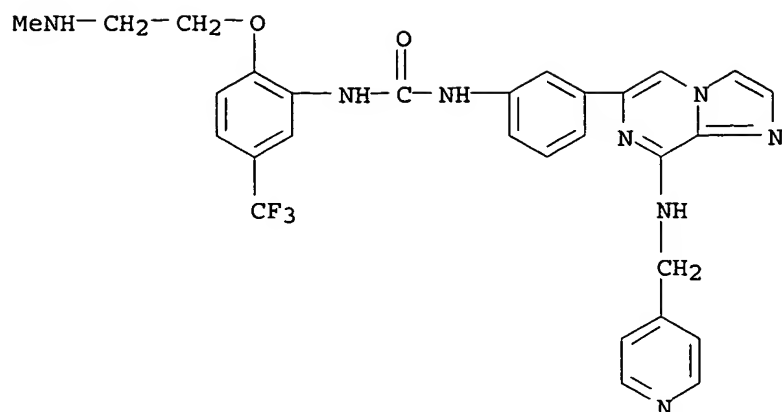
RN 847024-56-0 CAPLUS

CN Acetic acid, [2-[[[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]amino]-4-(trifluoromethyl)phenoxy]-(9CI) (CA INDEX NAME)



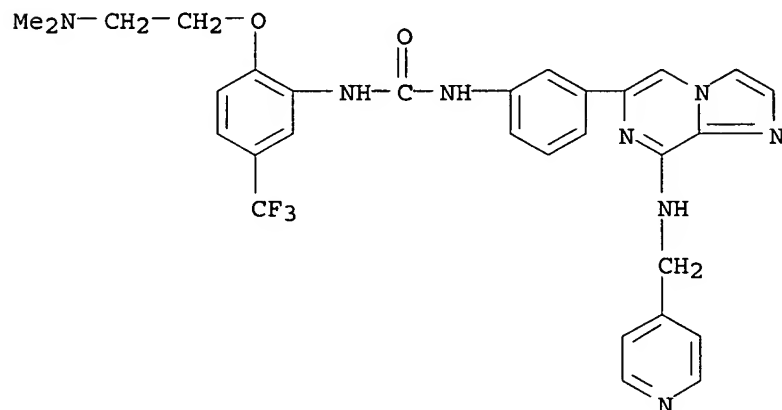
RN 847024-57-1 CAPLUS

CN Urea, N-[2-[2-(methyamino)ethoxy]-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



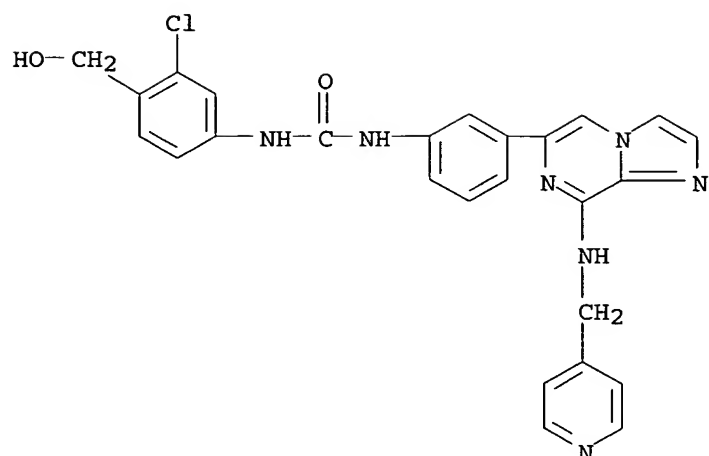
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CN Urea, N-[2-[2-(dimethylamino)ethoxy]-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



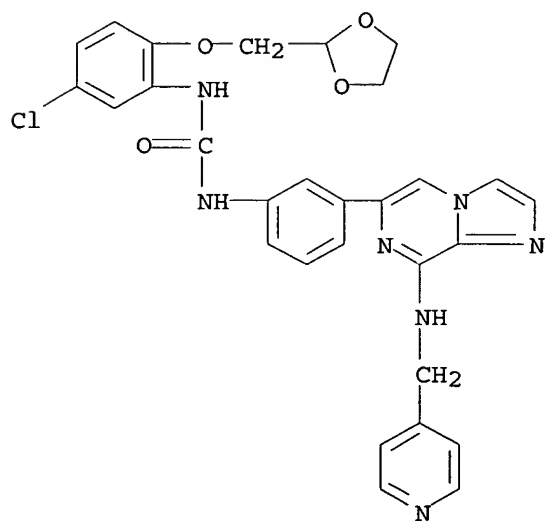
RN 847024-59-3 CAPLUS

CN Urea, N-[3-chloro-4-(hydroxymethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



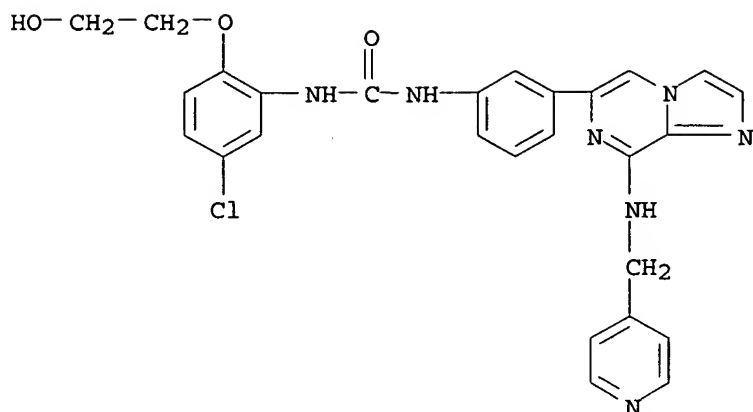
RN 847024-60-6 CAPLUS

CN Urea, N-[5-chloro-2-(1,3-dioxolan-2-ylmethoxy)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



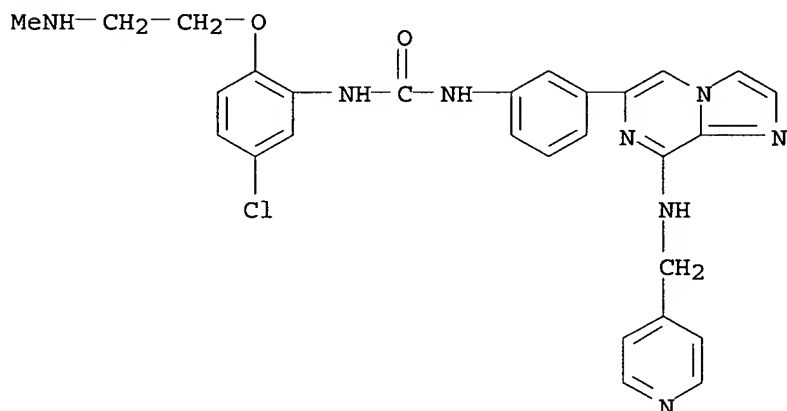
RN 847024-61-7 CAPLUS

CN Urea, N-[5-chloro-2-(2-hydroxyethoxy)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



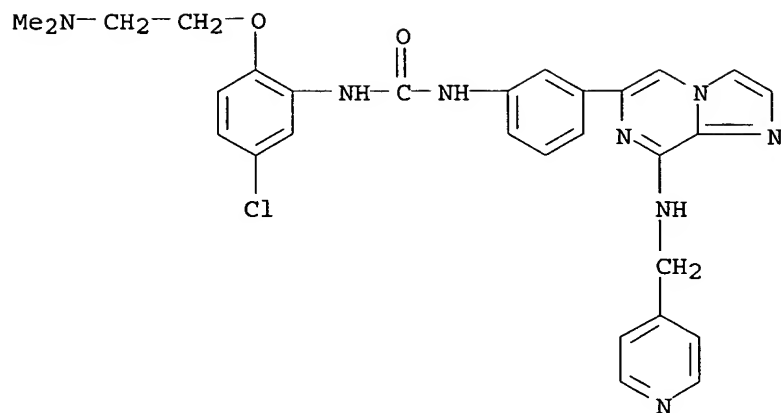
RN 847024-62-8 CAPLUS

CN Urea, N-[5-chloro-2-[2-(methylamino)ethoxy]phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



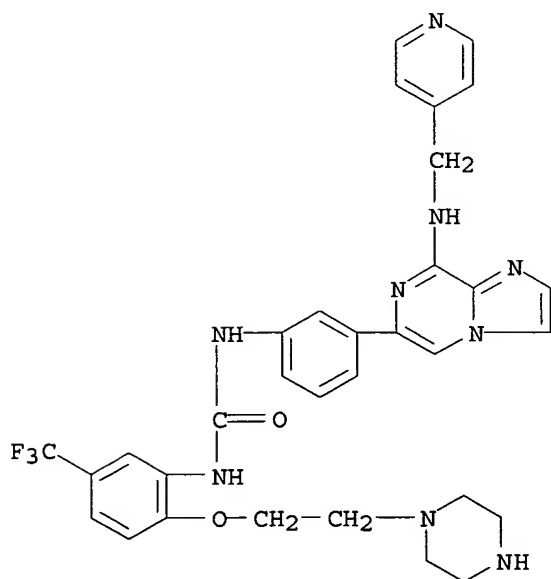
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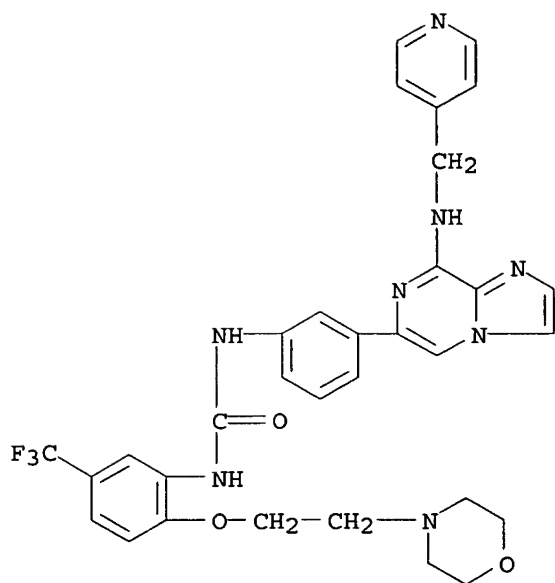
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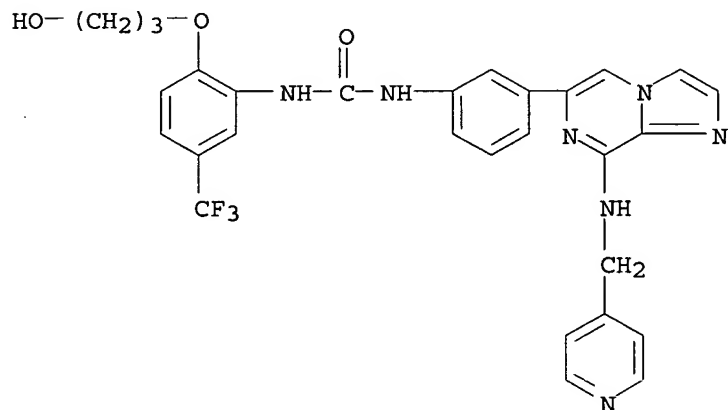
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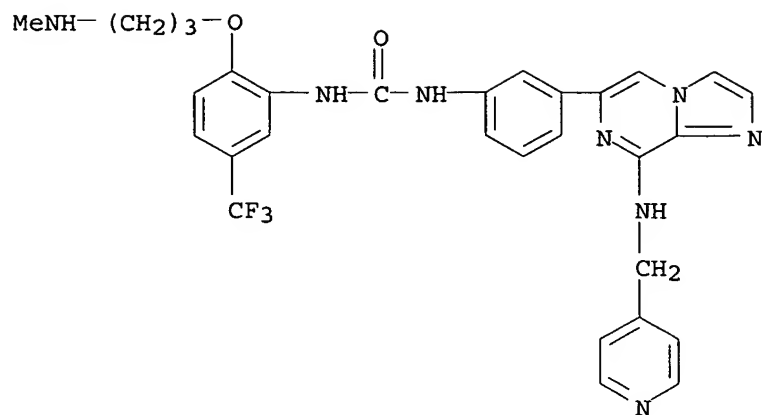
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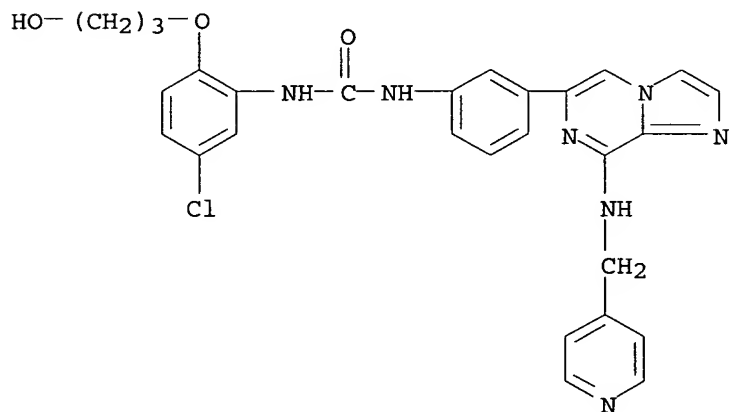
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CN Urea, N-[2-[3-(methyamino)propoxy]-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



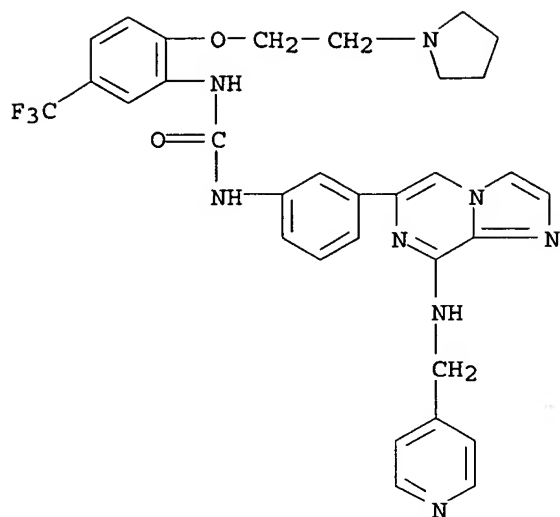
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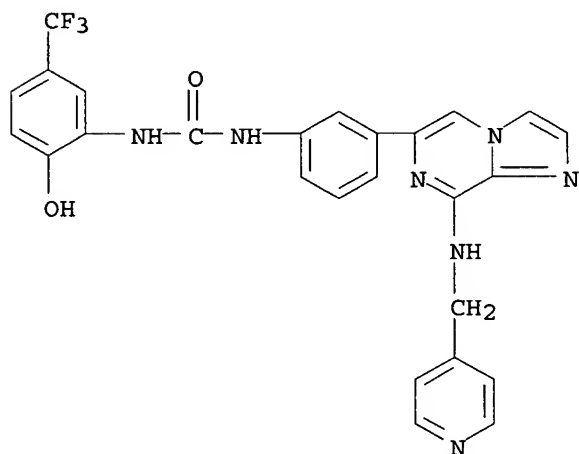
RN 847024-70-8 CAPLUS

CN Urea, N-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[2-[2-(1-pyrrolidinyl)ethoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 847024-71-9 CAPLUS

CN Urea, N-[2-hydroxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



L38 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:141072 CAPLUS

DOCUMENT NUMBER: 142:240469

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines for inhibition of bruton's tyrosine kinase

INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Mitchell, Scott A.; Pippin, Douglas A.; Darrow, James W.; Qian, Xiaobing; Velleca, Mark; Qian, Dapeng

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 181 pp.

CODEN: PIXXD2

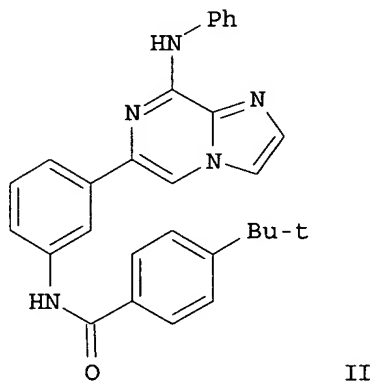
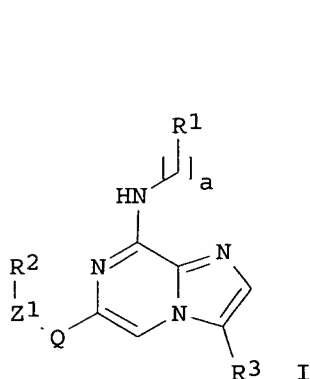
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014599	A1	20050217	WO 2004-US18227	20040604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005090499	A1	20050428	US 2004-861791	20040604
PRIORITY APPLN. INFO.:			US 2003-475634P	P 20030604
			US 2003-519311P	P 20031111
OTHER SOURCE(S):		MARPAT 142:240469		
ED Entered STN:		18 Feb 2005		
GI				



AB The title compds. I [a = 0-1; R¹ = substituted Ph, heteroaryl; R² = alkyl, alkoxyalkoxy, (heterocycloalkyl)alkyl, (cycloalkyl)alkyl, etc.; Z¹ = CONR⁴, NR⁴CO; R⁴ = H, alkyl, cycloalkyl, etc.; Q = Ph, pyridyl; R³ = H, halo, alkyl, etc.], useful for treating diseases responsive to inhibition of Btk activity and/or B-cell proliferation such as cancer, an autoimmune and/or inflammatory disease, or an acute inflammatory reaction, were prepared E.g., a multi-step synthesis of II (no characterization data for intermediates), starting from 3,5-dibromo-2-aminopyrazine, was given. The exemplified compds. I were tested in the Btk biochem. assay and found to exhibit an IC₅₀ value less than or equal to 1 μM. Pharmaceutical compns. containing one or more compds. I, or a pharmaceutically acceptable form of such compds., and one or more pharmaceutically acceptable carriers, excipients, or diluents are provided herein. Other embodiments include methods of treating human and animals, including livestock and domesticated companion animals, suffering from a disease responsive to inhibition of Btk activity. Methods of treatment include administering a compound I as a single active agent or administering a compound I in

combination with one or more other therapeutic agent. A method for determining the presence of Btk in a sample, comprising contacting the sample with a compound I under conditions that permit detection of Btk activity, detecting a level of Btk activity in the sample, and therefrom determining the presence

or

absence of Btk in the sample, is also disclosed.

IT

845269-72-9P 845269-73-0P 845269-74-1P
845269-75-2P 845269-77-4P 845269-79-6P
845269-80-9P 845269-81-0P 845269-82-1P
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845271-34-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazo[1,2-a]pyrazin-8-ylamines for inhibition of bruton's tyrosine kinase)

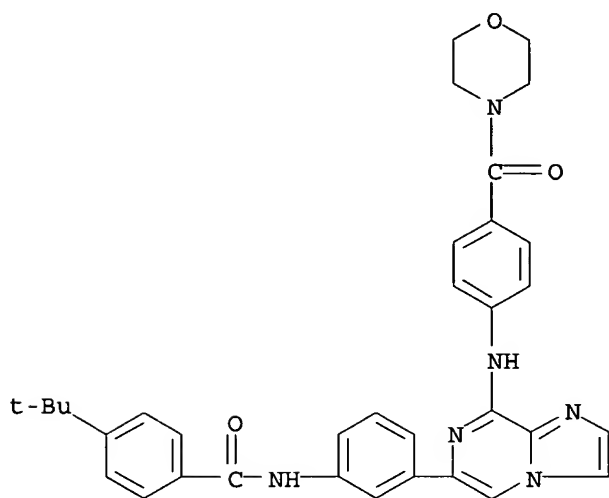
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845269-72-9 CAPLUS

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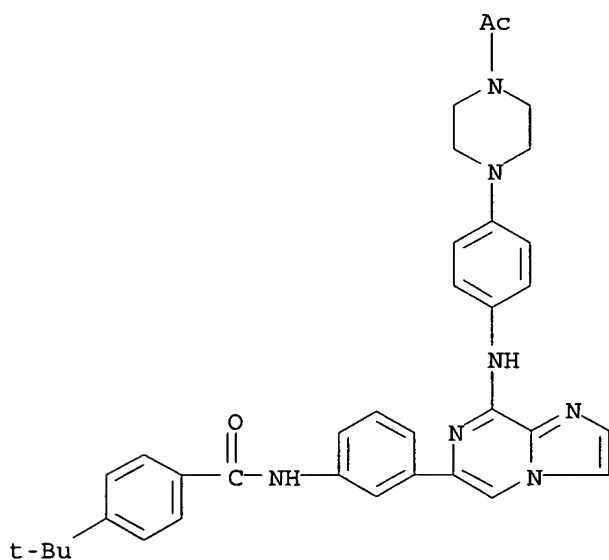
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(CA INDEX NAME)



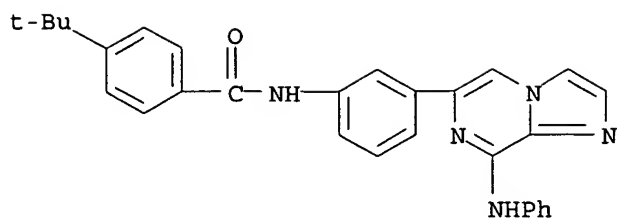
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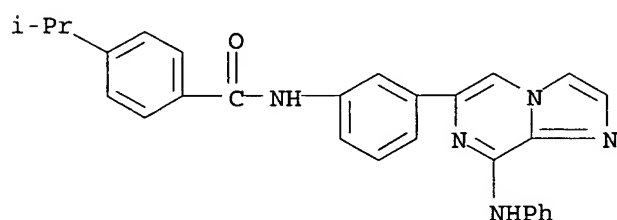
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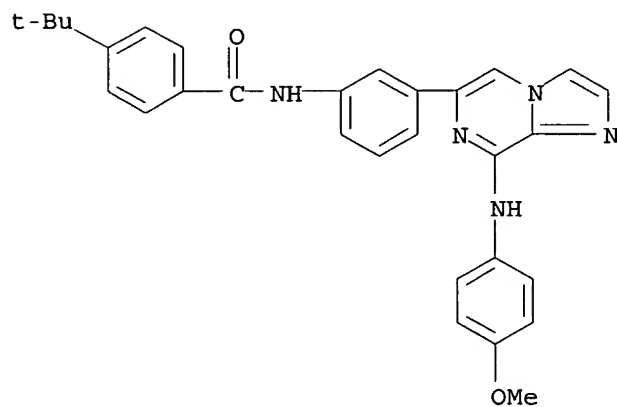
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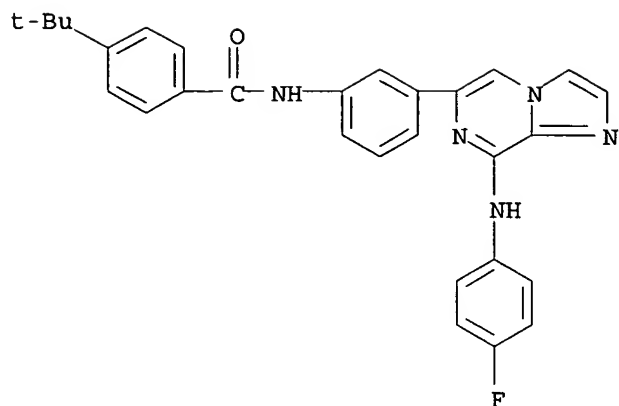
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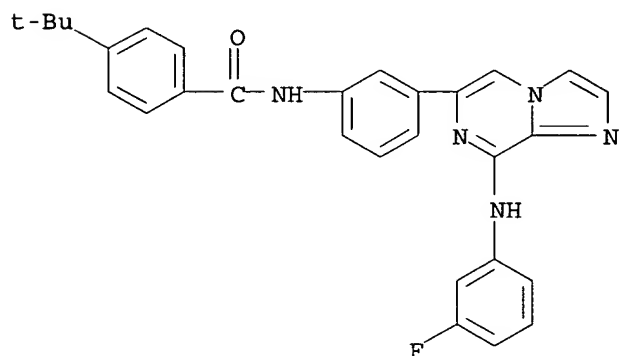
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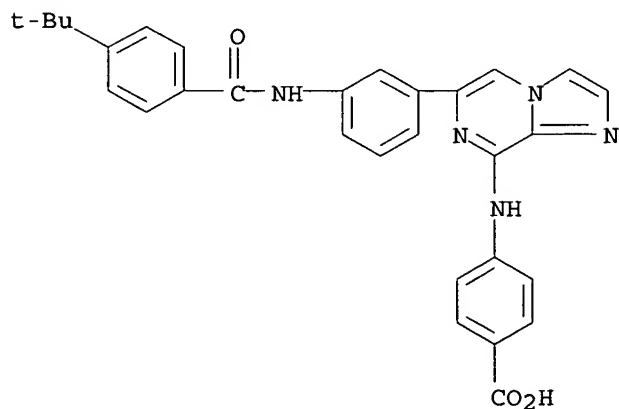
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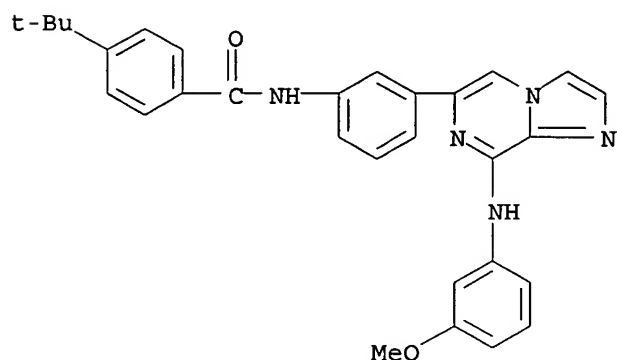
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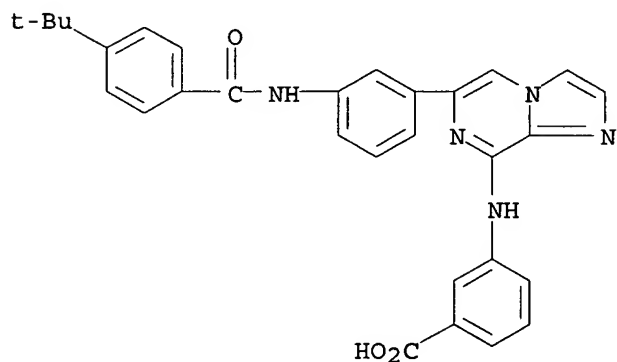
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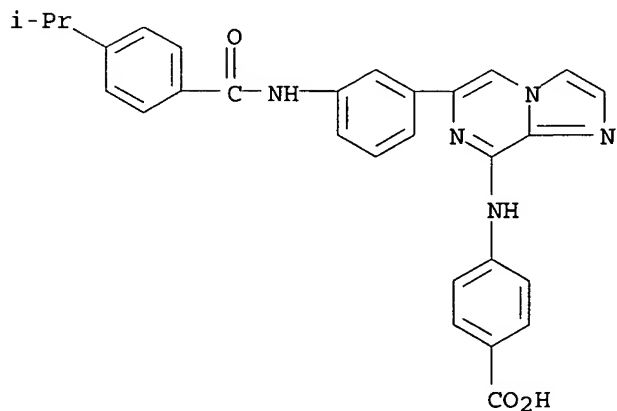
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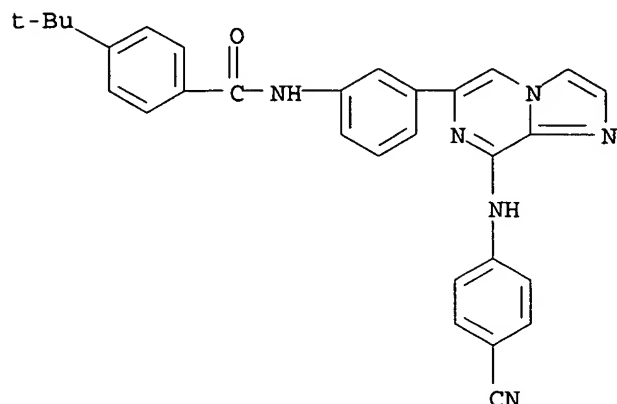
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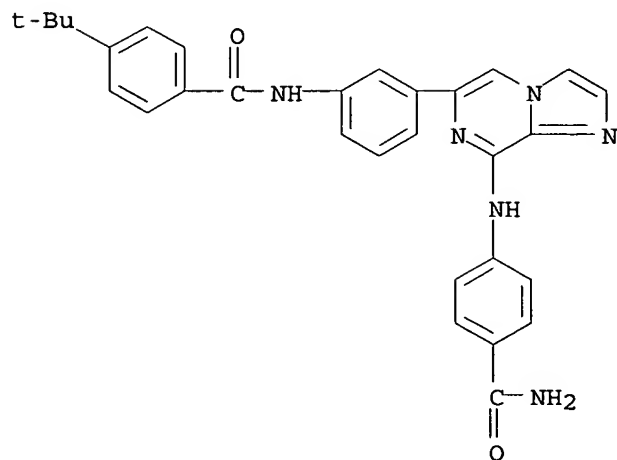
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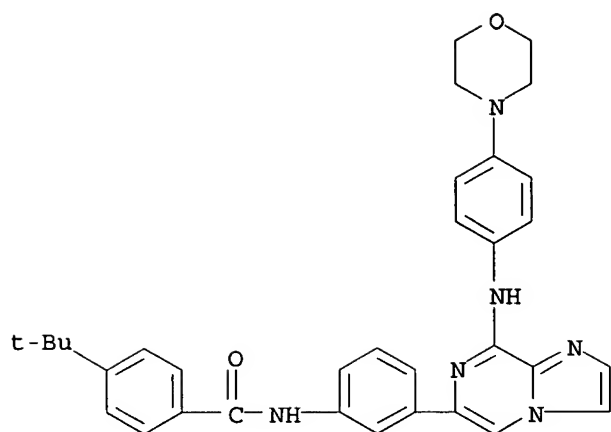
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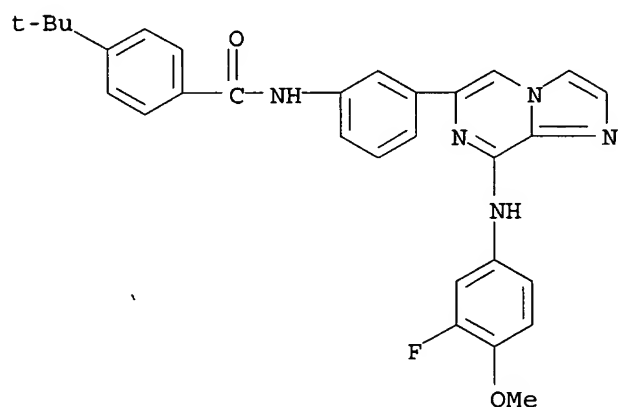
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CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



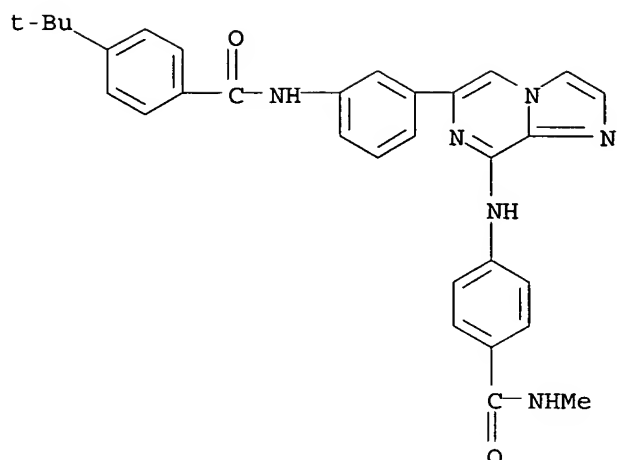
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CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(3-fluoro-4-methoxyphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



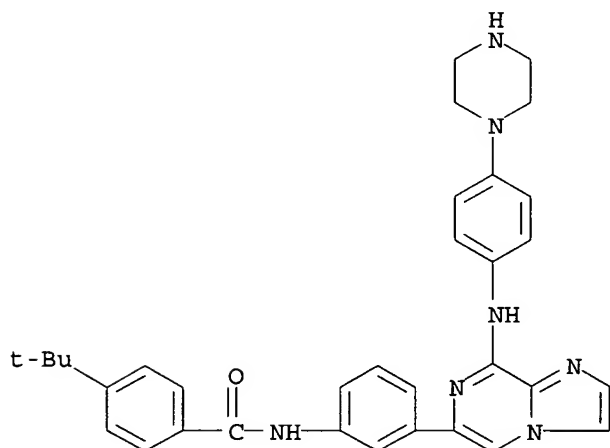
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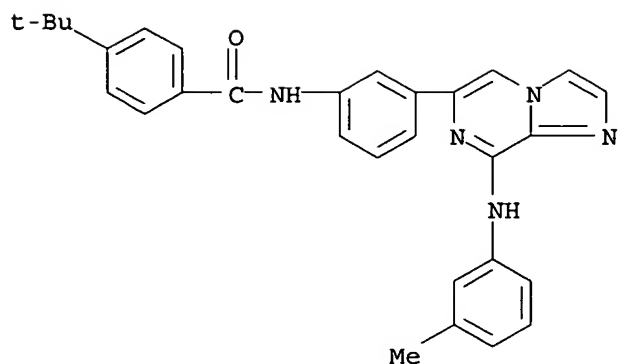
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CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



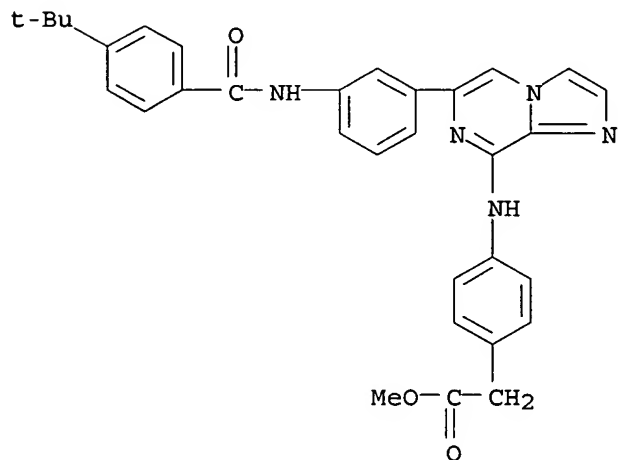
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CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(3-methylphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



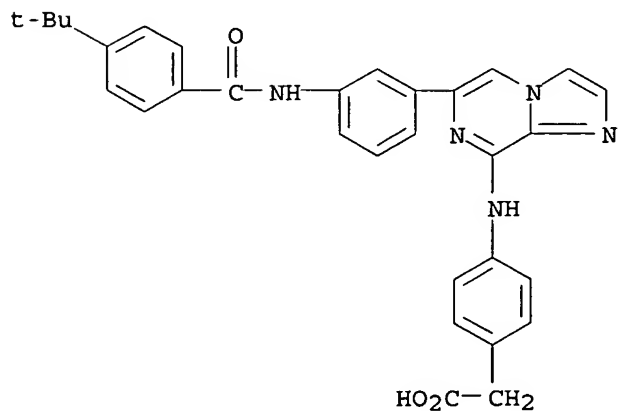
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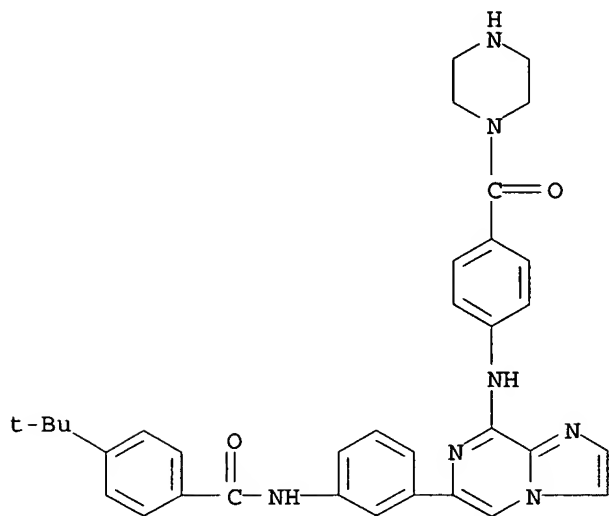


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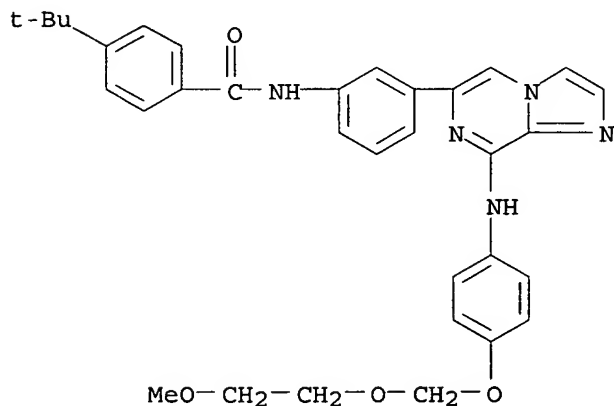
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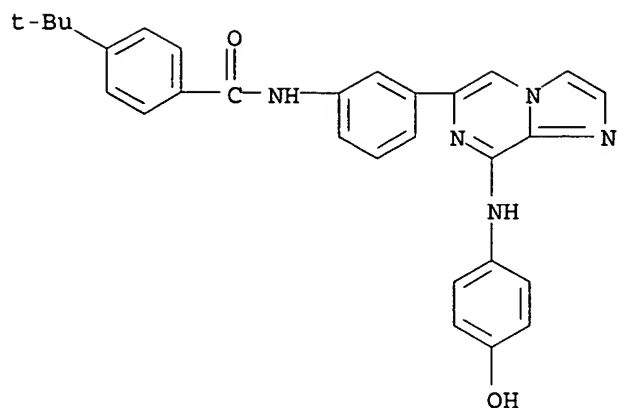
RN 845269-95-6 CAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-piperazinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
 (CA INDEX NAME)



RN 845269-96-7 CAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(2-methoxyethoxy)methoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)

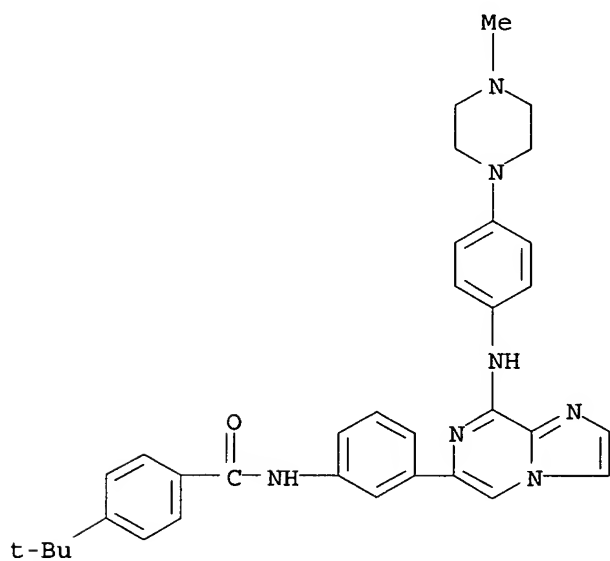


RN 845269-97-8 CAPLUS
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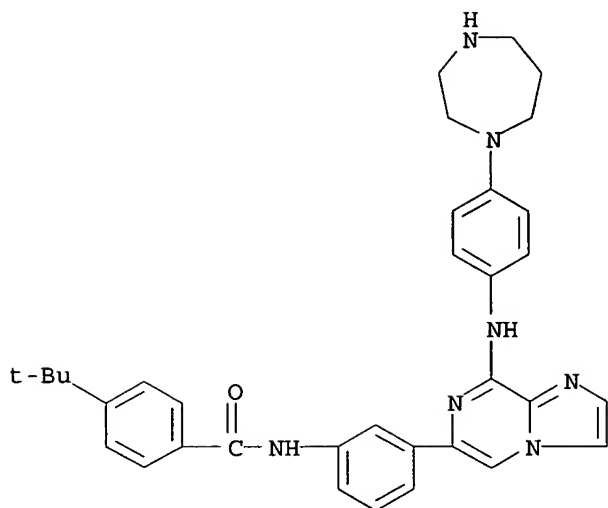
RN 845269-99-0 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-methyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



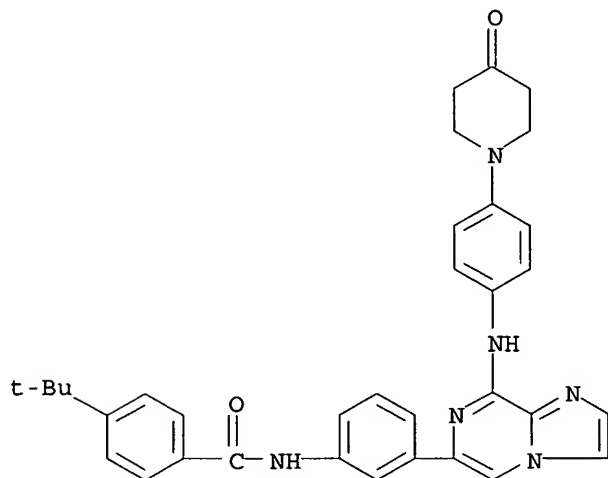
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CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(hexahydro-1H-1,4-diazepin-1-yl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



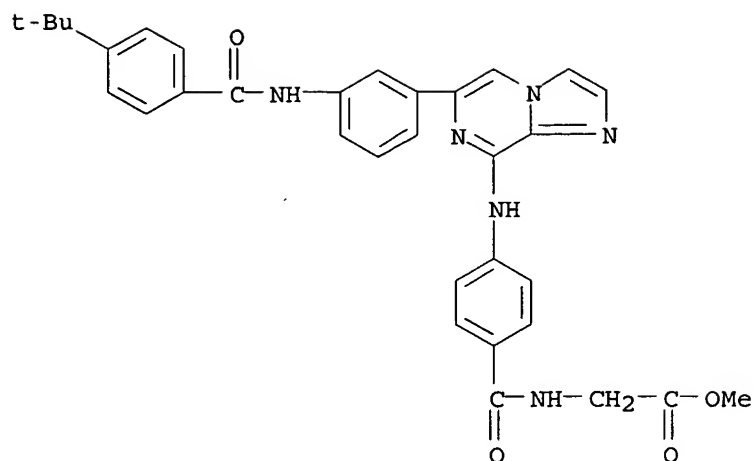
RN 845270-01-1 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-oxo-1-piperidinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



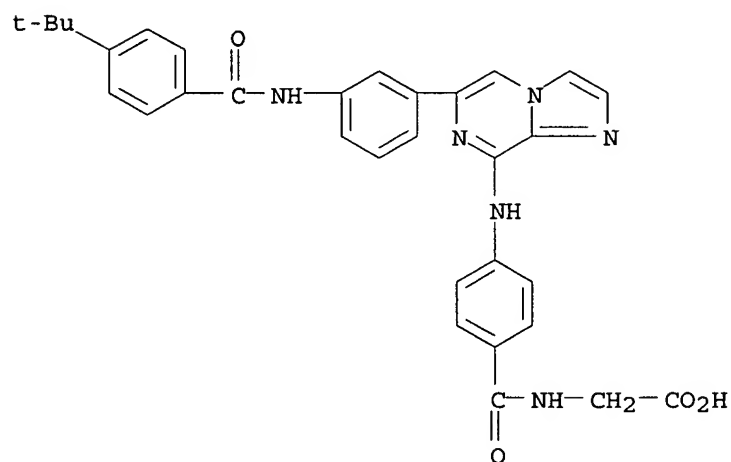
RN 845270-02-2 CAPLUS

CN Glycine, N-[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]-, methyl ester (9CI) (CA INDEX NAME)



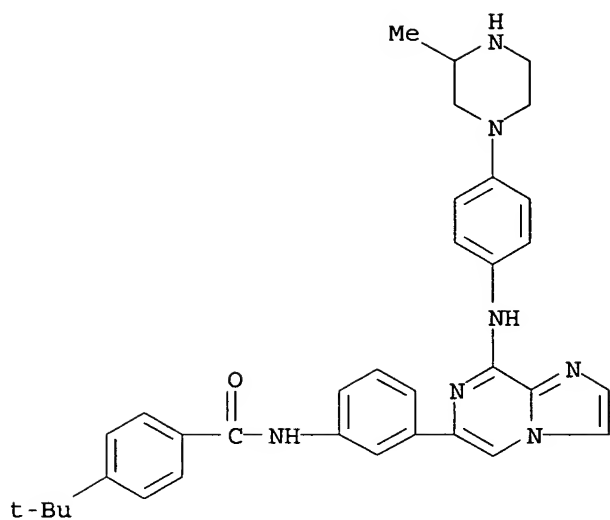
RN 845270-03-3 CAPLUS

CN Glycine, N-[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]- (9CI) (CA INDEX NAME)



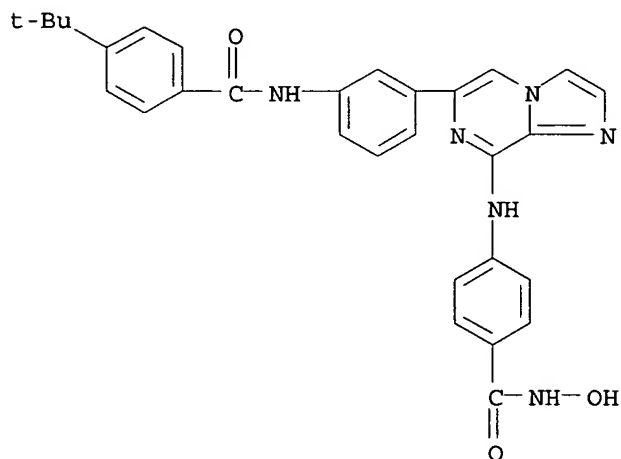
RN 845270-04-4 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(3-methyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



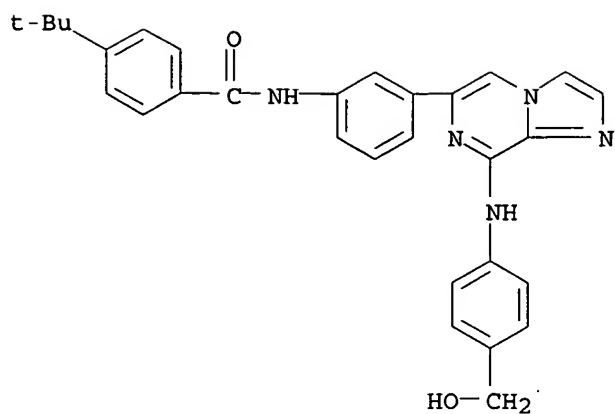
RN 845270-05-5 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-hydroxy-phenyl]benzamide (9CI) (CA INDEX NAME)

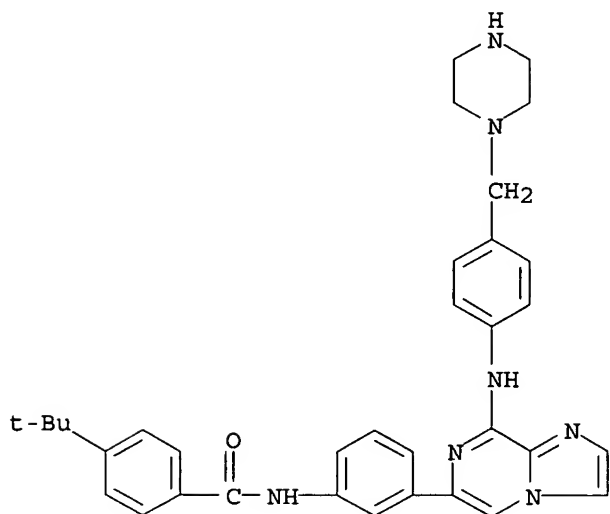


RN 845270-06-6 CAPLUS

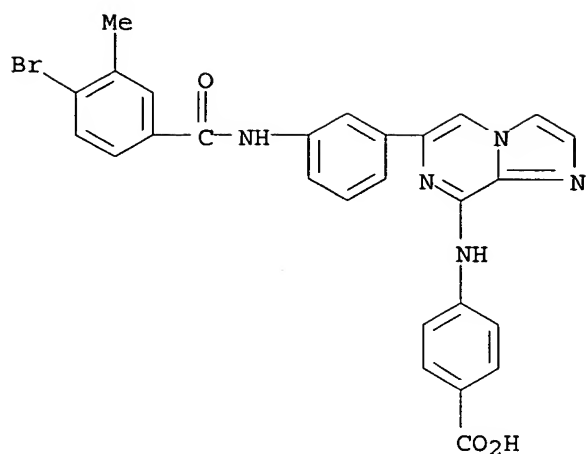
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(hydroxymethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845270-07-7 CAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-piperazinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
 (CA INDEX NAME)

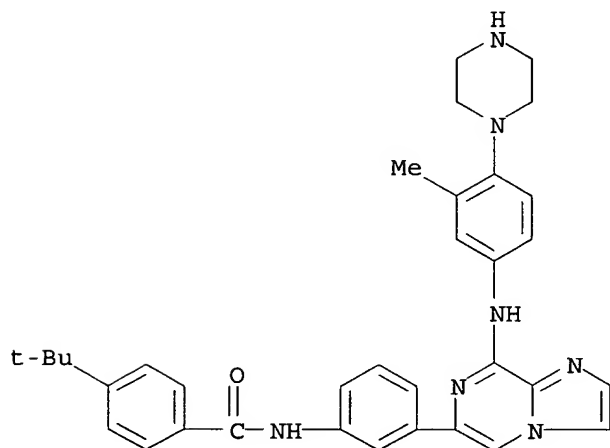


RN 845270-08-8 CAPLUS
 CN Benzoic acid, 4-[[6-[3-[(4-bromo-3-methylbenzoyl)amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino] - (9CI) (CA INDEX NAME)



RN 845270-09-9 CAPLUS

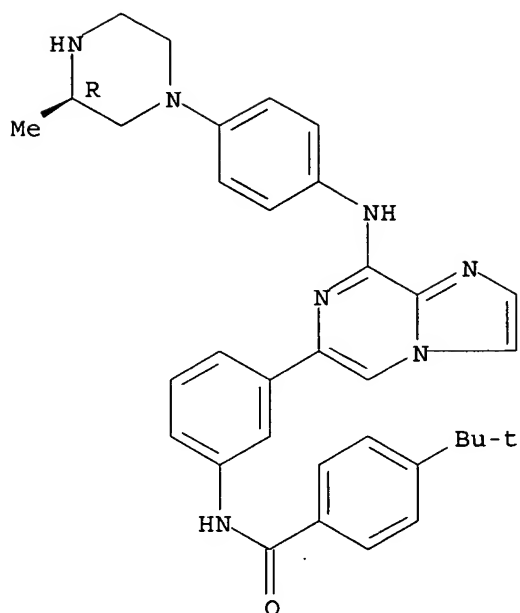
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-methyl-4-(1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845270-10-2 CAPLUS

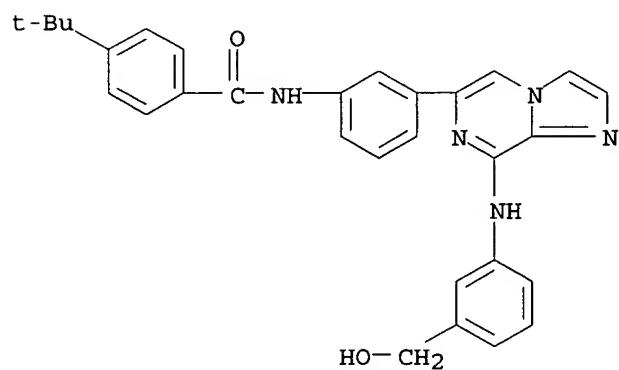
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3R)-3-methyl-1-piperazinyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 845270-11-3 CAPLUS

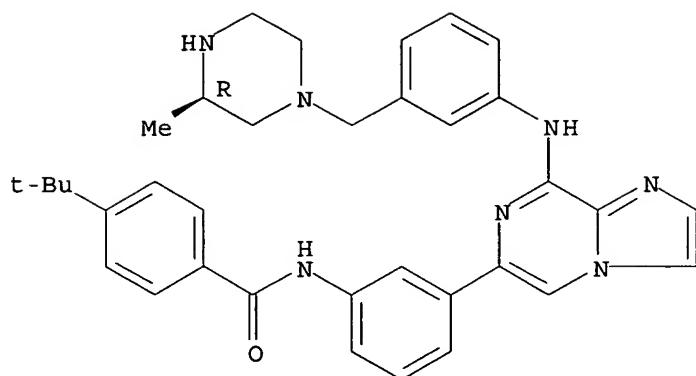
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-(hydroxymethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845270-12-4 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-[[3-[(3R)-3-methyl-1-piperazinyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

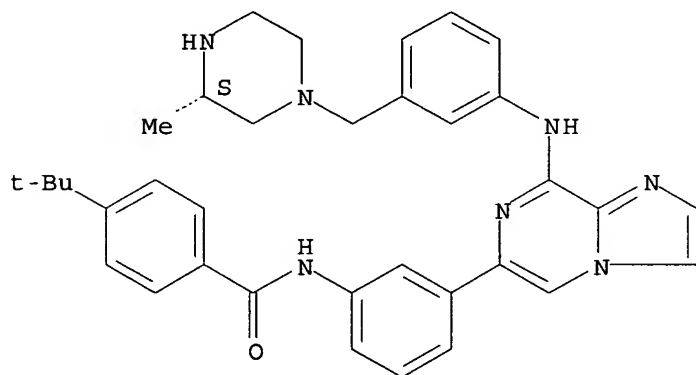
Absolute stereochemistry.



RN 845270-13-5 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-[[[(3S)-3-methyl-1-piperazinyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)

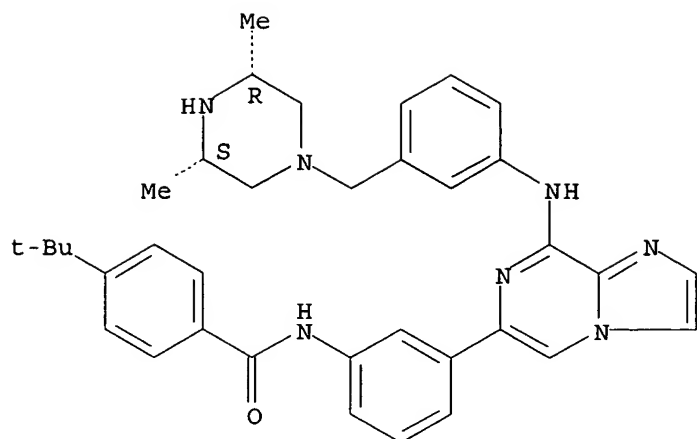
Absolute stereochemistry.



RN 845270-14-6 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-[[[(3R,5S)-3,5-dimethyl-1-piperazinyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

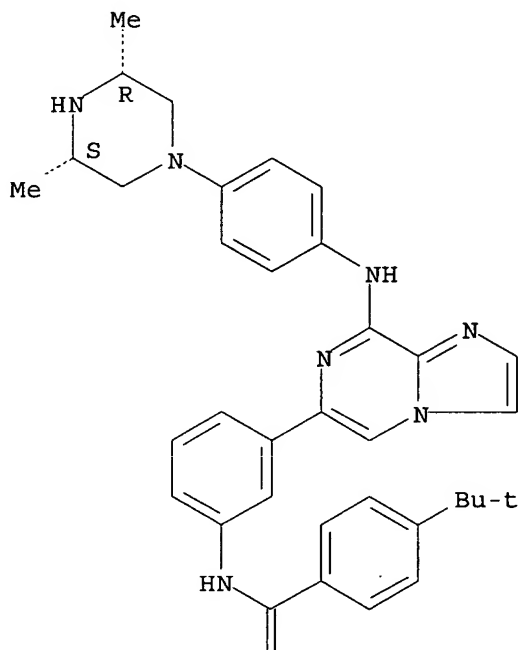


RN 845270-15-7 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3R,5S)-3,5-dimethyl-1-piperazinyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-, rel- (9CI)
(CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

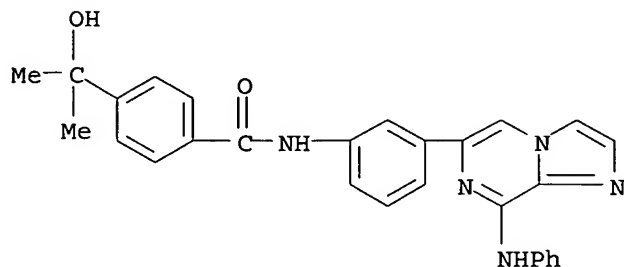


PAGE 2-A



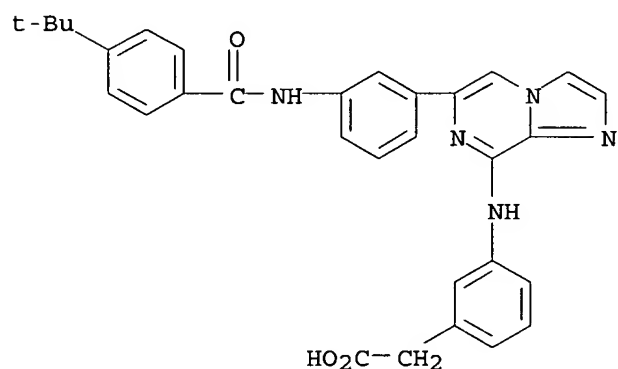
RN 845270-17-9 CAPLUS

CN Benzamide, 4-(1-hydroxy-1-methylethyl)-N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



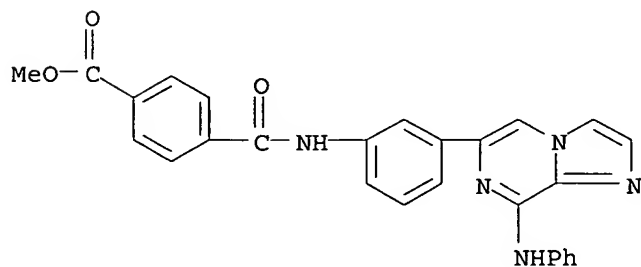
RN 845270-18-0 CAPLUS

CN Benzeneacetic acid, 3-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



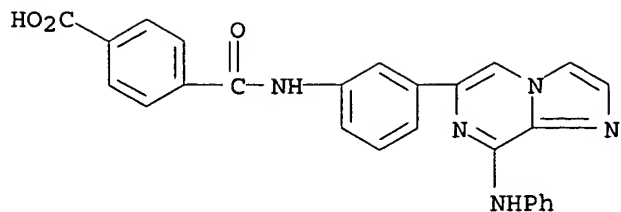
RN 845270-19-1 CAPLUS

CN Benzoic acid, 4-[[[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



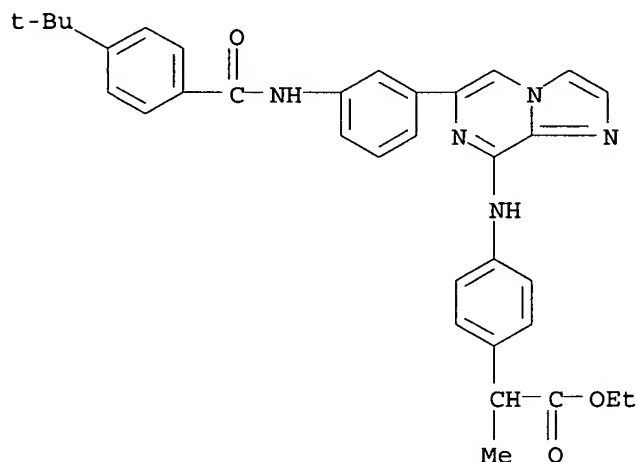
RN 845270-20-4 CAPLUS

CN Benzoic acid, 4-[[[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



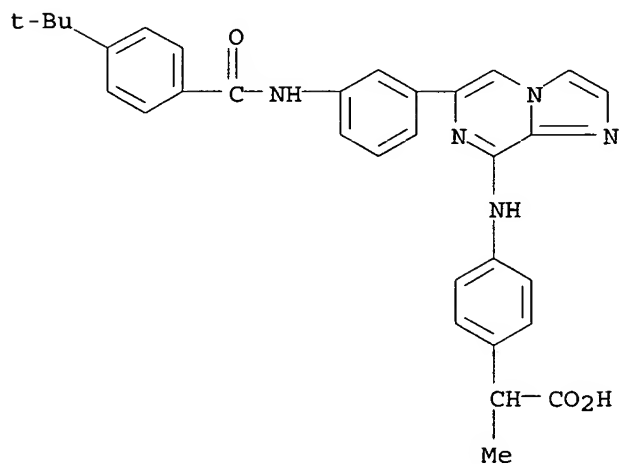
RN 845270-21-5 CAPLUS

CN Benzeneacetic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-α-methyl-, ethyl ester (9CI) (CA INDEX NAME)



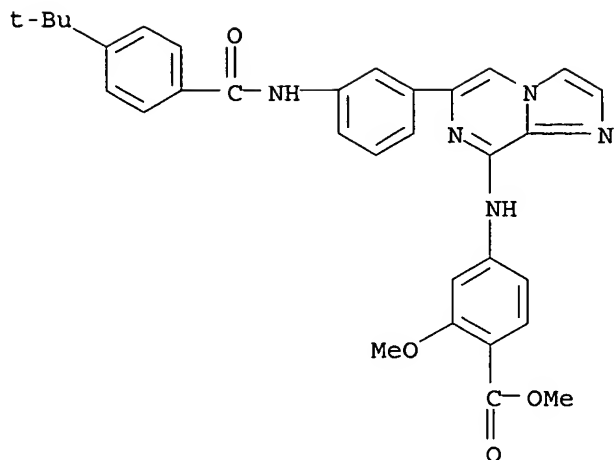
RN 845270-22-6 CAPLUS

CN Benzeneacetic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-α-methyl- (9CI) (CA INDEX NAME)



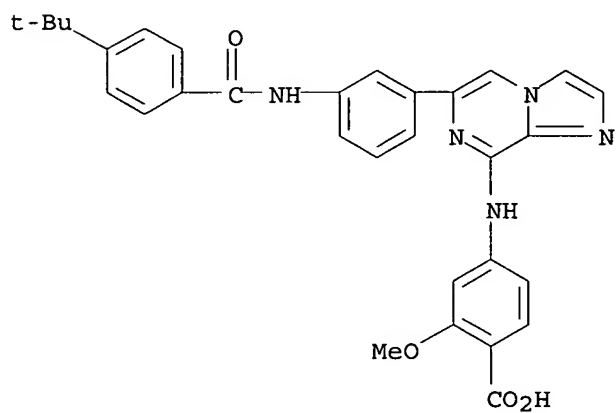
RN 845270-23-7 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methoxy-, methyl ester (9CI) (CA INDEX NAME)



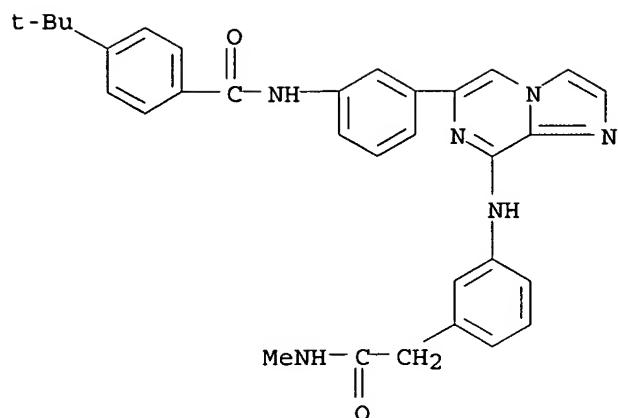
RN 845270-24-8 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methoxy- (9CI) (CA INDEX NAME)



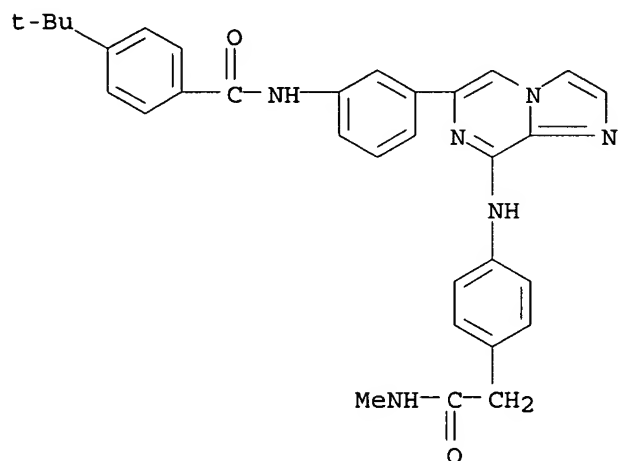
RN 845270-25-9 CAPLUS

CN Benzeneacetamide, 3-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl- (9CI) (CA INDEX NAME)



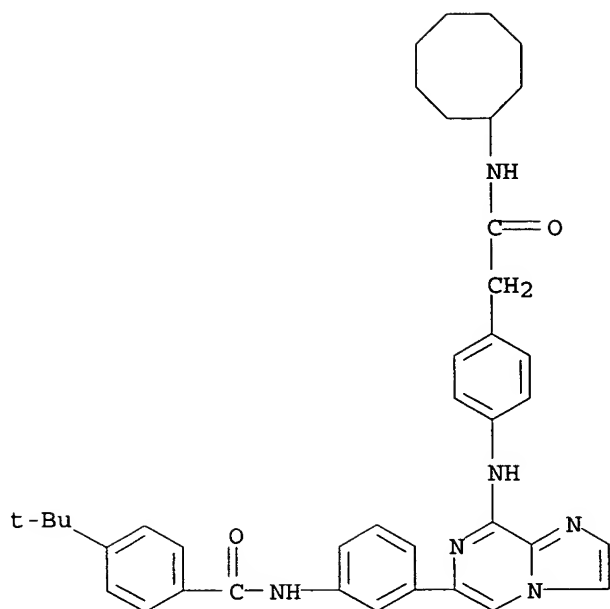
RN 845270-26-0 CAPLUS

CN Benzeneacetamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl- (9CI) (CA INDEX NAME)



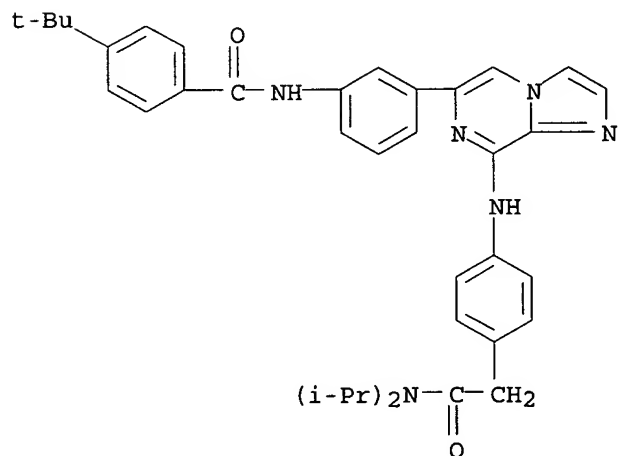
RN 845270-27-1 CAPLUS

CN Benzeneacetamide, N-cyclooctyl-4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



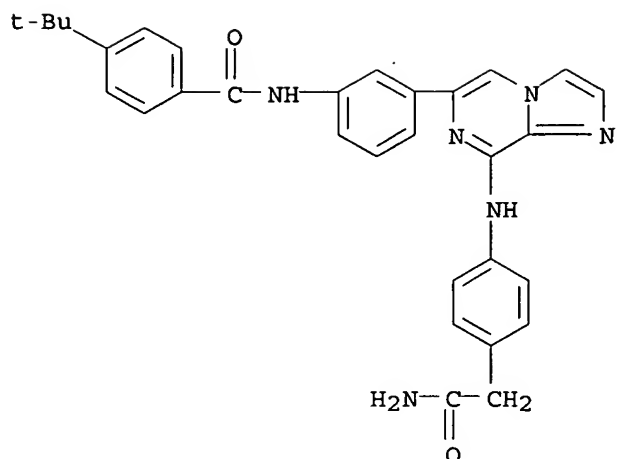
RN 845270-28-2 CAPLUS

CN Benzeneacetamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-bis(1-methylethyl)- (9CI) (CA INDEX NAME)



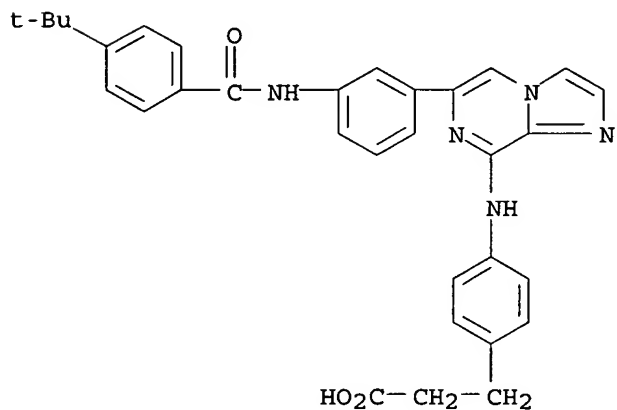
RN 845270-29-3 CAPLUS

CN Benzeneacetamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



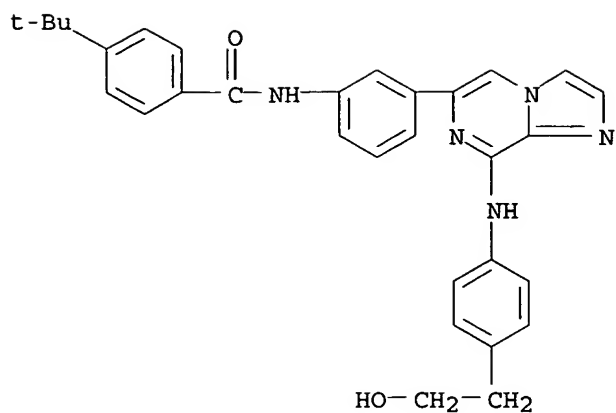
RN 845270-30-6 CAPLUS

CN Benzenepropanoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



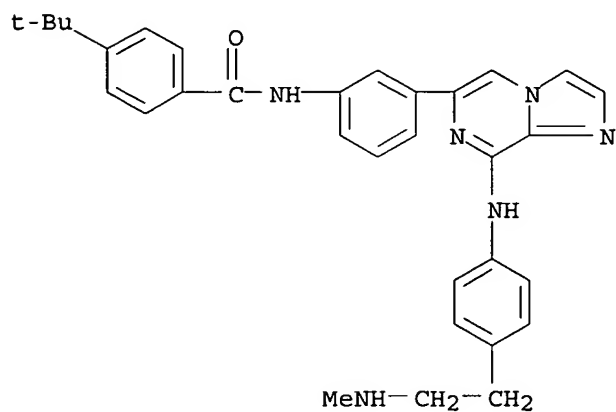
RN 845270-31-7 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(2-hydroxyethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



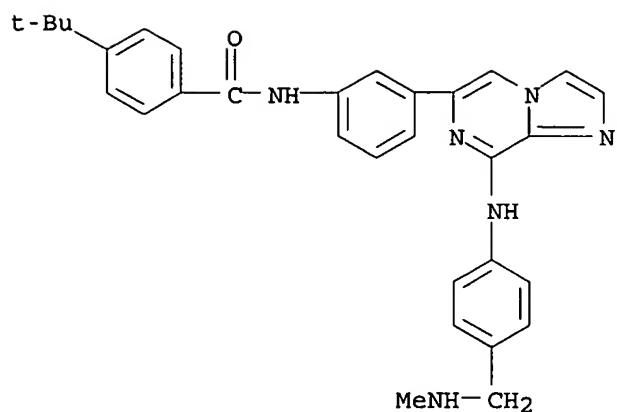
RN 845270-32-8 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-(methylamino)ethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



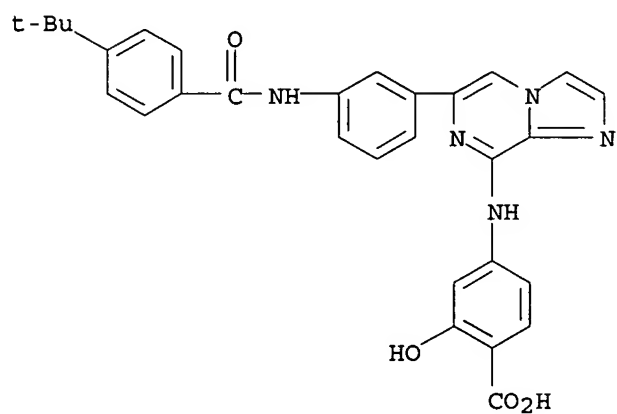
RN 845270-33-9 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(methylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



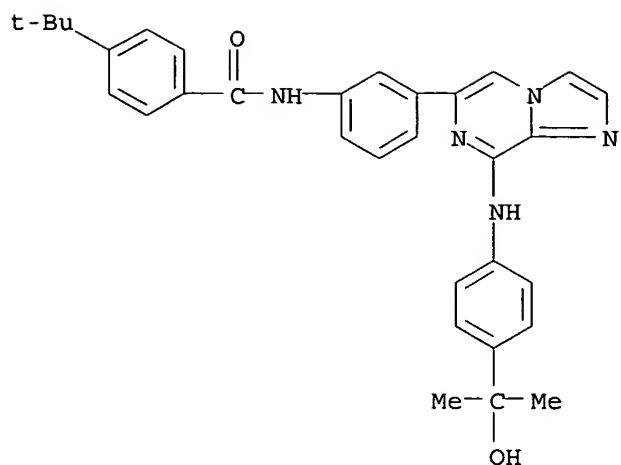
RN 845270-34-0 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)



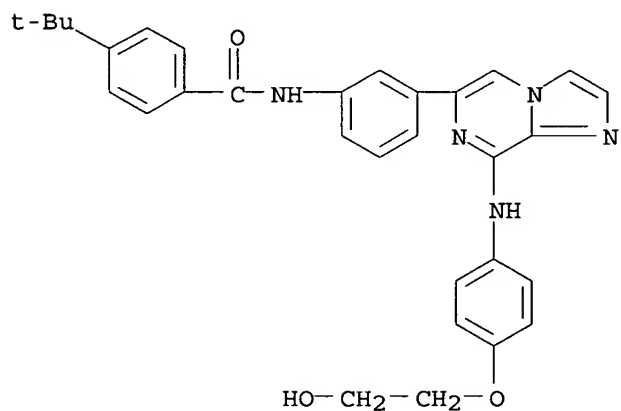
RN 845270-35-1 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-hydroxy-1-methylethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



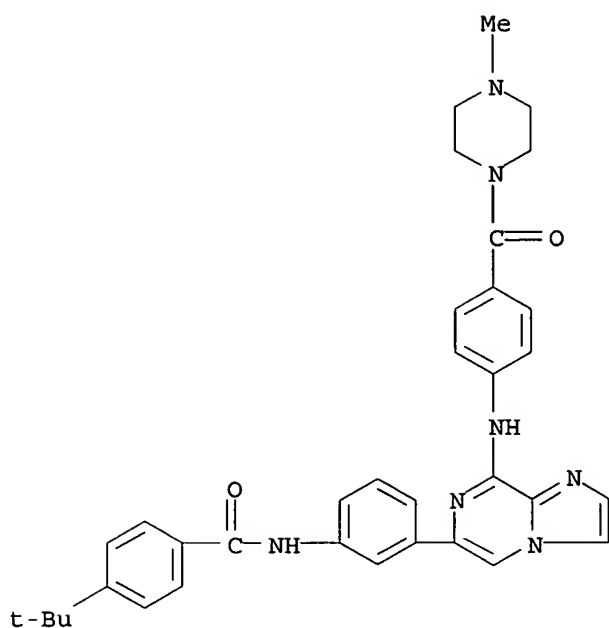
RN 845270-36-2 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(2-hydroxyethoxy)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



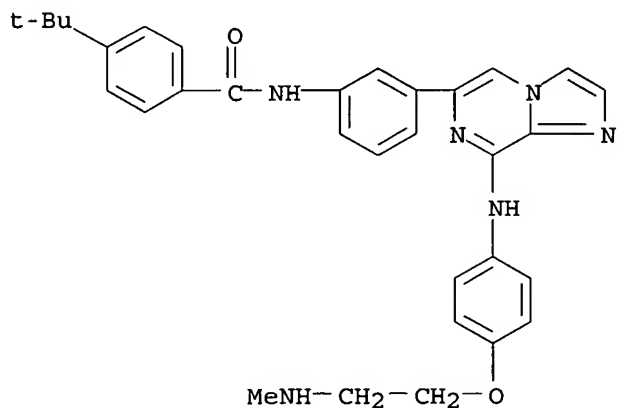
RN 845270-37-3 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(4-methyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



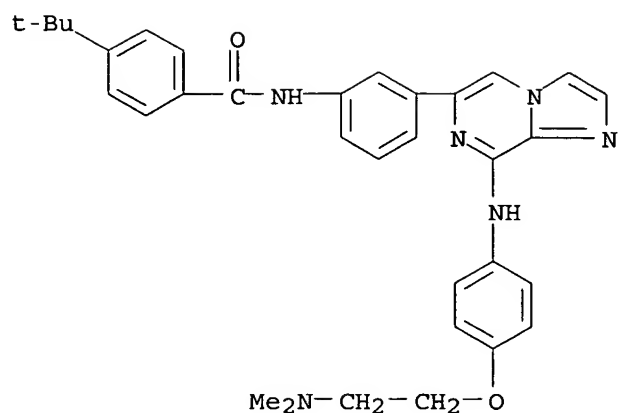
RN 845270-38-4 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-(methylamino)ethoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



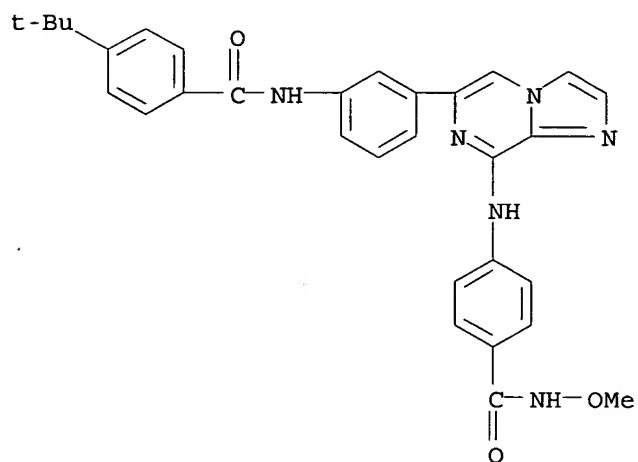
RN 845270-39-5 CAPLUS

CN Benzamide, N-[3-[8-[[4-[2-(dimethylamino)ethoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



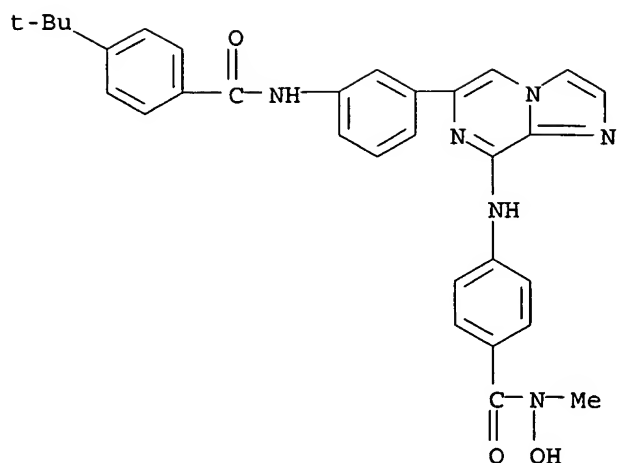
RN 845270-40-8 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methoxy- (9CI) (CA INDEX NAME)



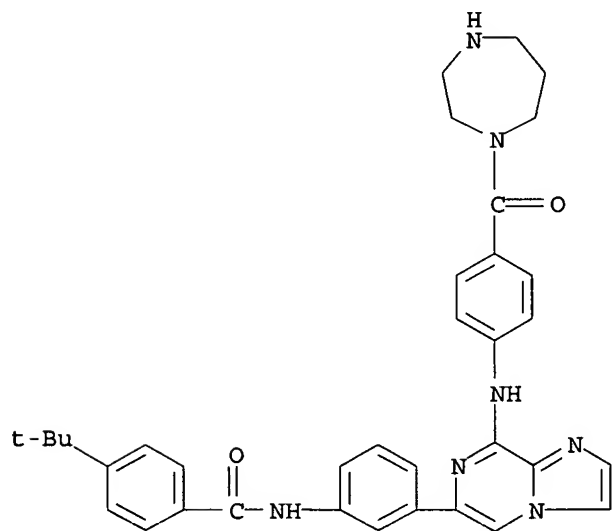
RN 845270-41-9 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-hydroxy-N-methyl- (9CI) (CA INDEX NAME)



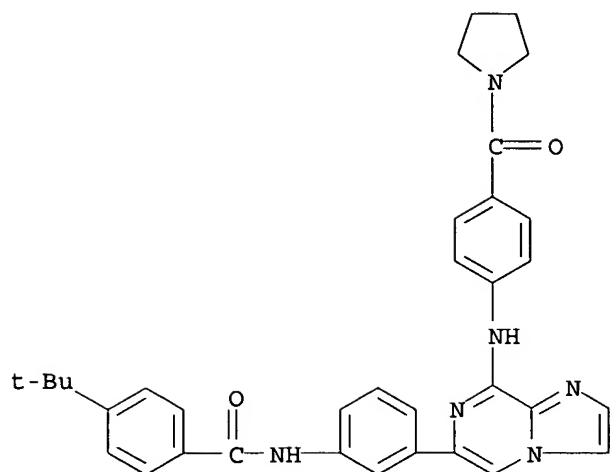
RN 845270-42-0 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(hexahydro-1H-1,4-diazepin-1-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



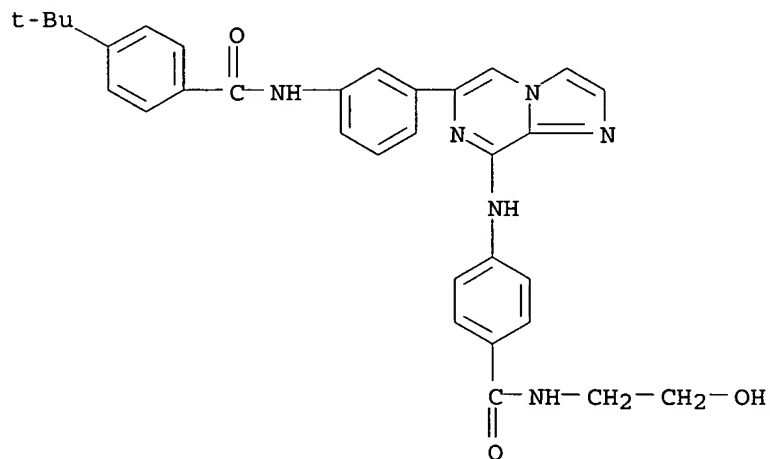
RN 845270-43-1 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-pyrrolidinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



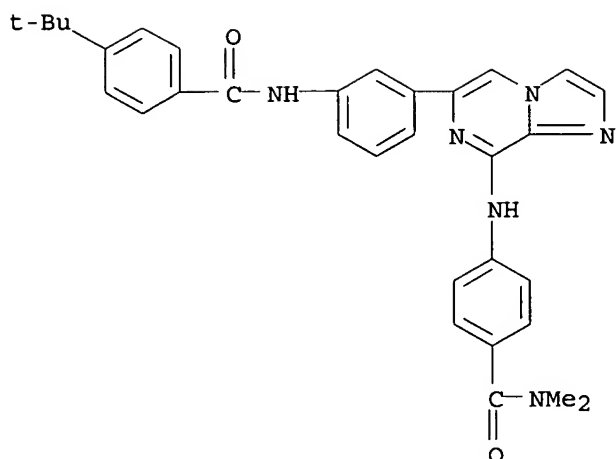
RN 845270-44-2 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



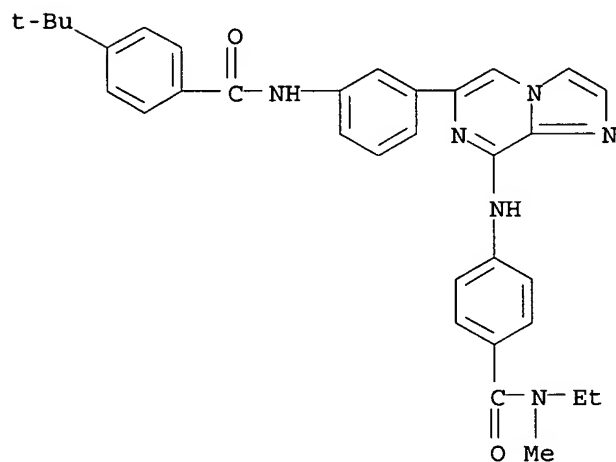
RN 845270-45-3 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl- (9CI) (CA INDEX NAME)



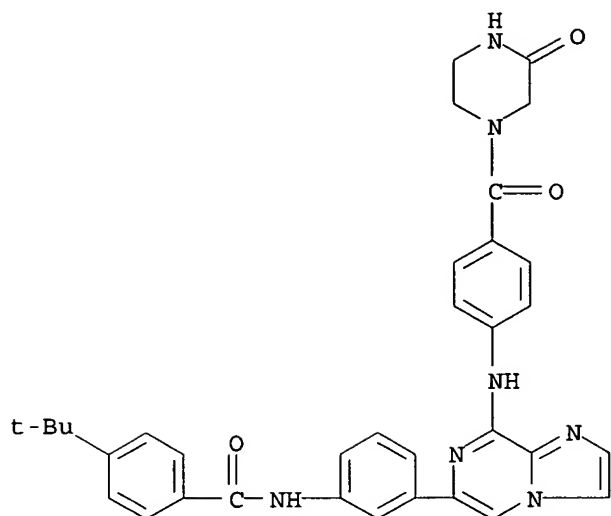
RN 845270-46-4 CAPLUS

CN Benzamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-ethyl-N-methyl- (9CI) (CA INDEX NAME)



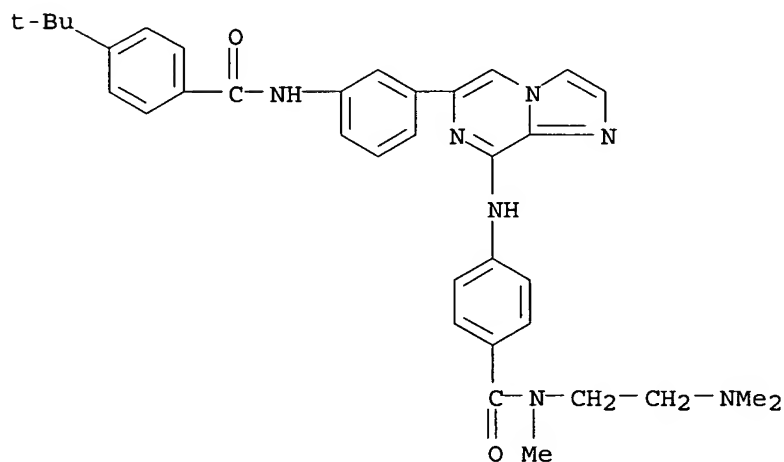
RN 845270-47-5 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide (9CI) (CA INDEX NAME)



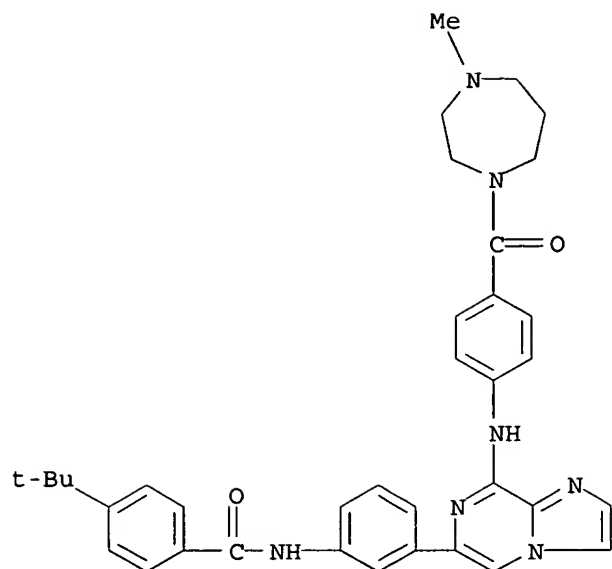
RN 845270-48-6 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl- (9CI) (CA INDEX NAME)



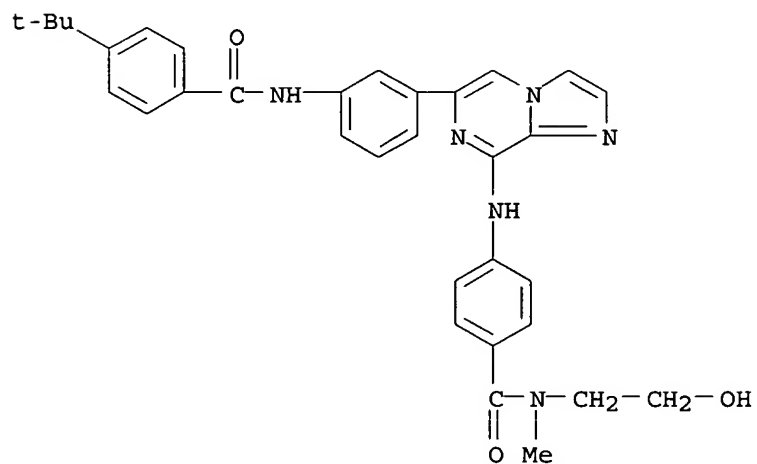
RN 845270-49-7 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



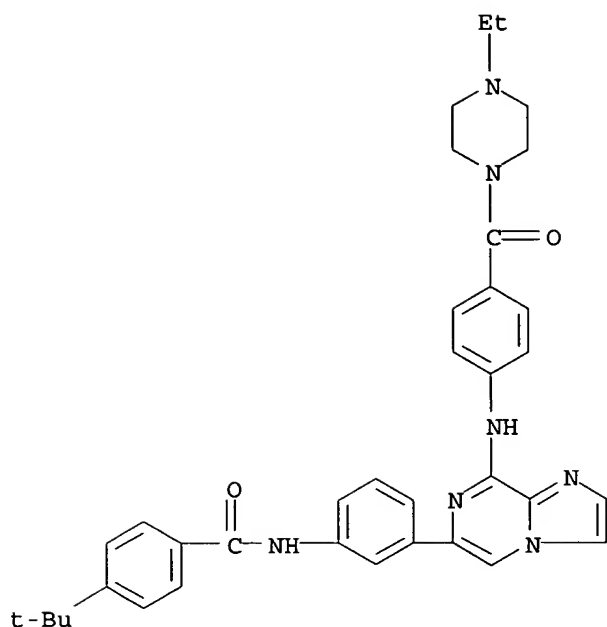
RN 845270-50-0 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)-N-methyl- (9CI) (CA INDEX NAME)



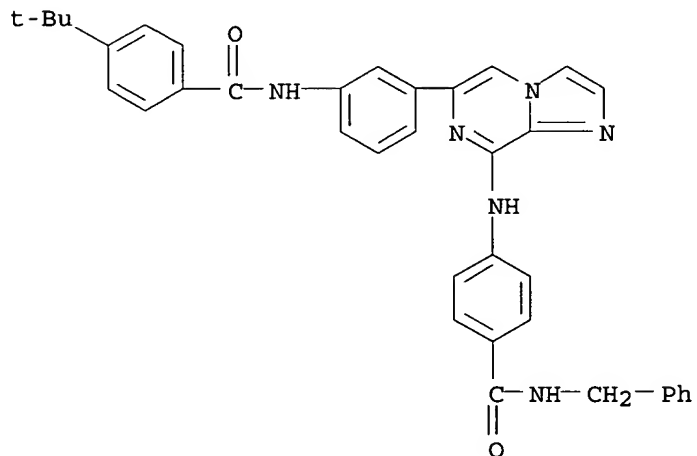
RN 845270-51-1 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(4-ethyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



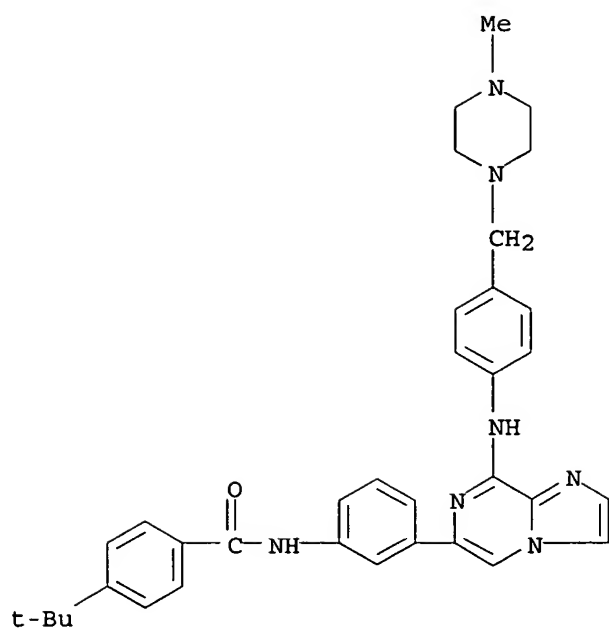
RN 845270-52-2 CAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



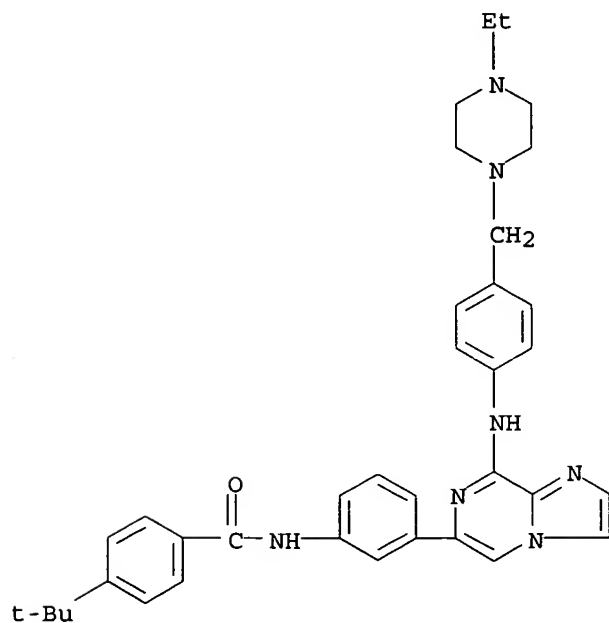
RN 845270-54-4 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[[4-[[4-methyl-1-piperazinyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



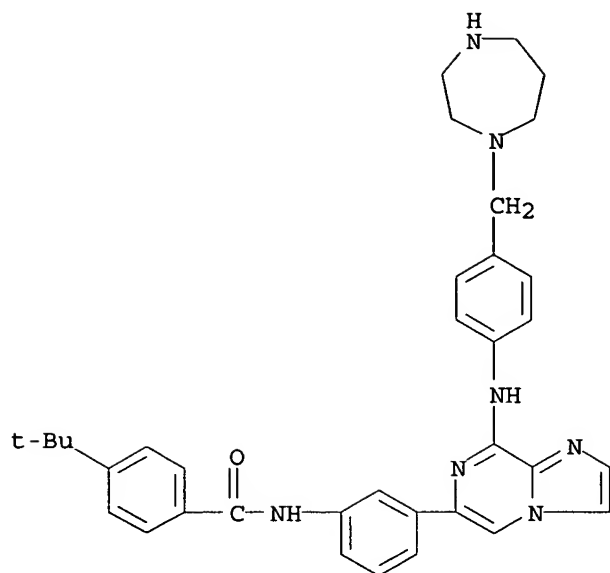
RN 845270-56-6 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(4-ethyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



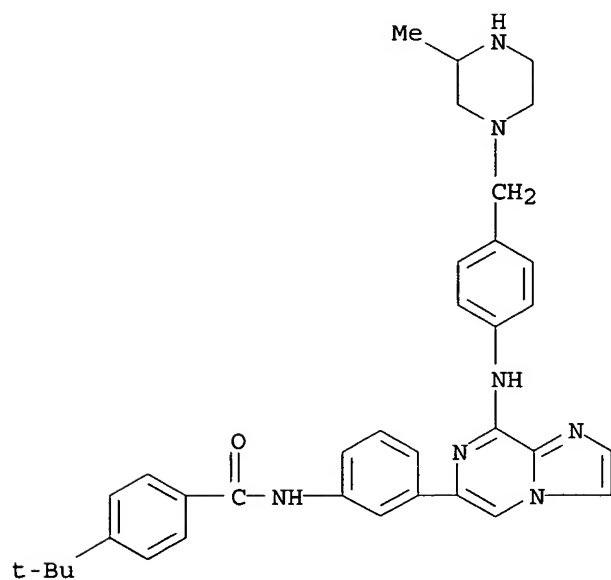
RN 845270-57-7 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(hexahydro-1H-1,4-diazepin-1-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



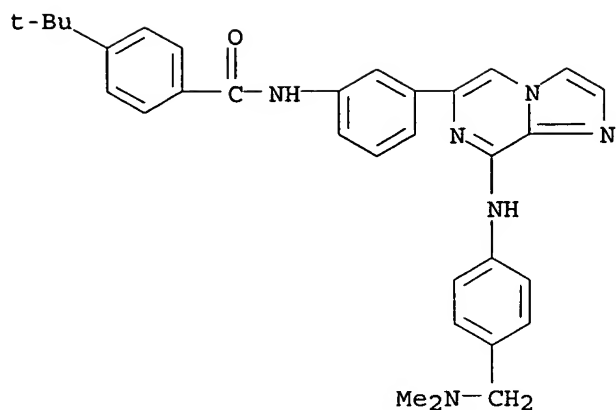
RN 845270-58-8 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3-methyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



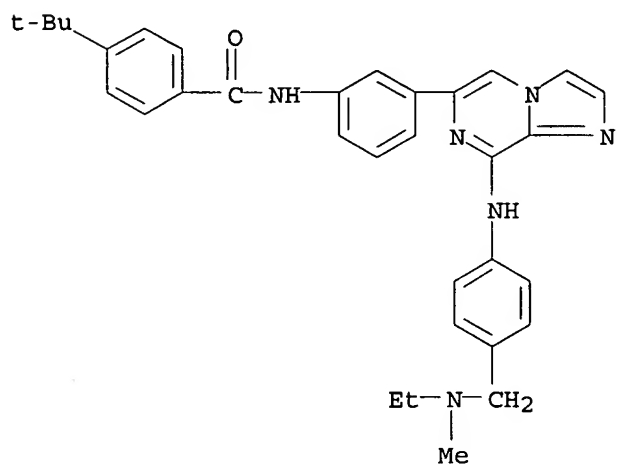
RN 845270-59-9 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(dimethylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



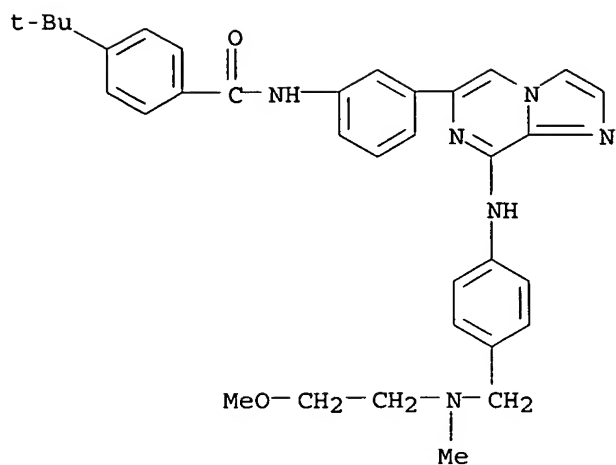
RN 845270-60-2 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(ethylmethylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



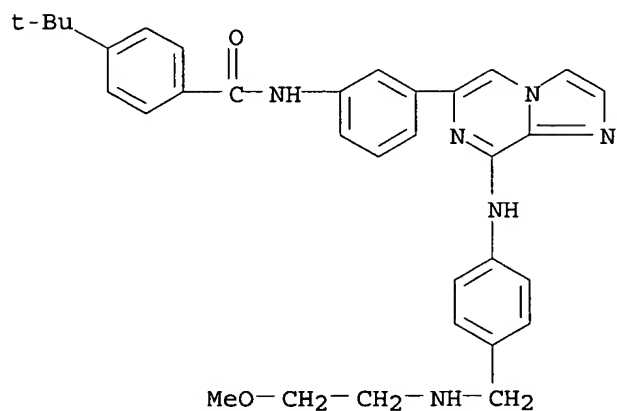
RN 845270-61-3 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[2-methoxyethyl)methylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



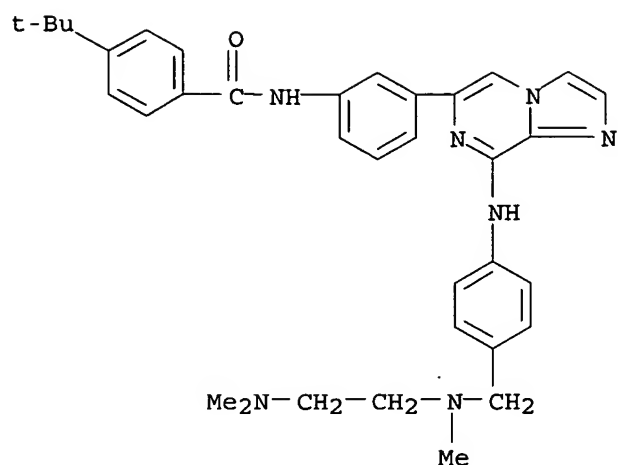
RN 845270-62-4 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[2-methoxyethyl]amino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



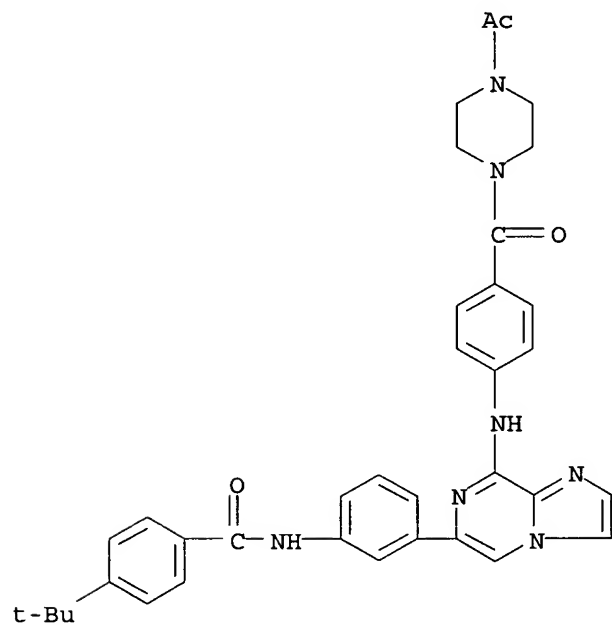
RN 845270-63-5 CAPLUS

CN Benzamide, N-[3-[8-[[4-[[2-(dimethylamino)ethyl]methylamino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)-(9CI) (CA INDEX NAME)



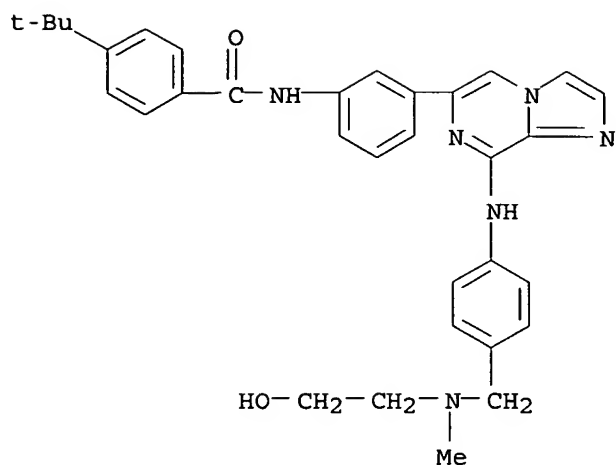
RN 845270-64-6 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(4-acetyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



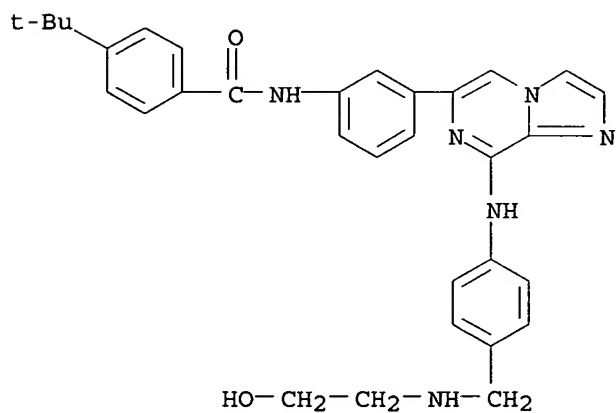
RN 845270-65-7 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[[(2-hydroxyethyl)methylamino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



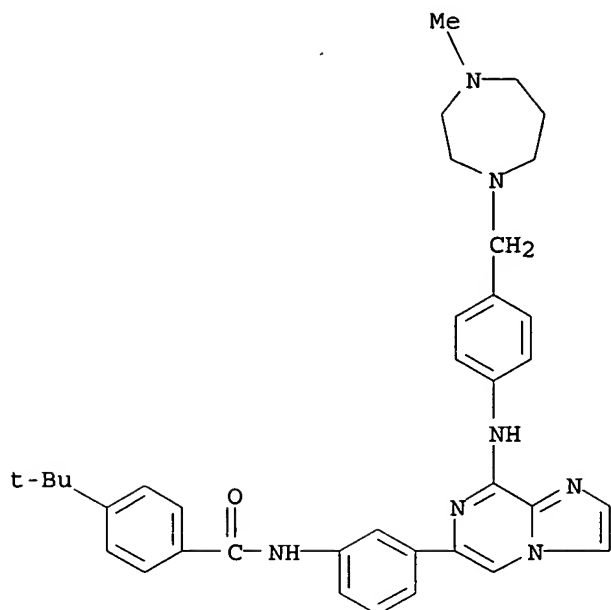
RN 845270-66-8 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(2-hydroxyethyl)amino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



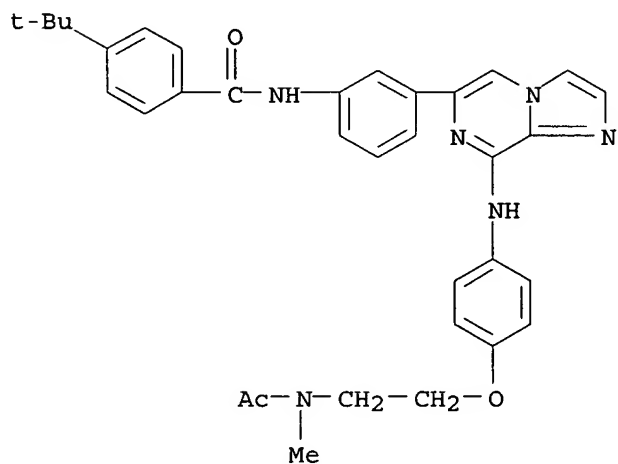
RN 845270-67-9 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



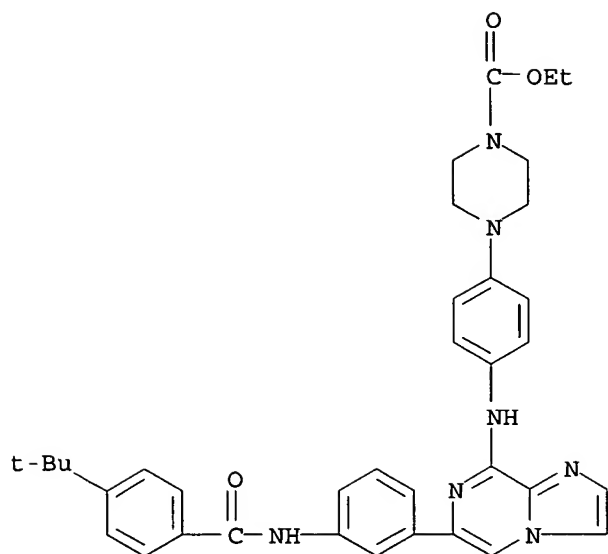
RN 845270-68-0 CAPLUS

CN Benzamide, N-[3-[8-[[4-[2-(acetylmethylamino)ethoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



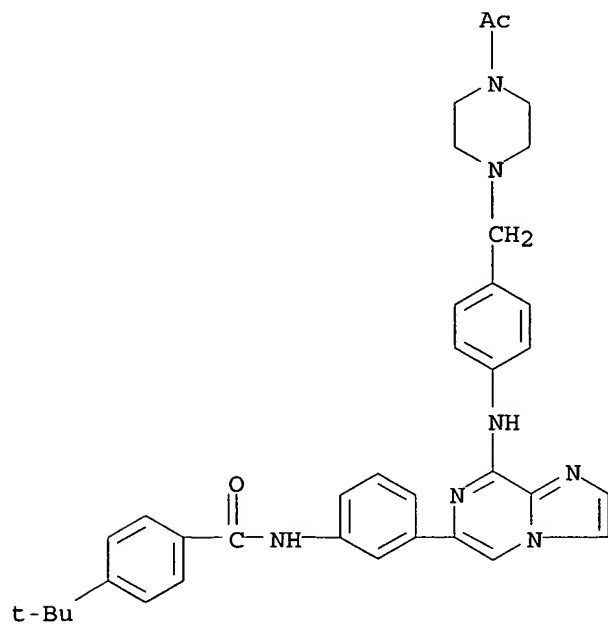
RN 845270-69-1 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



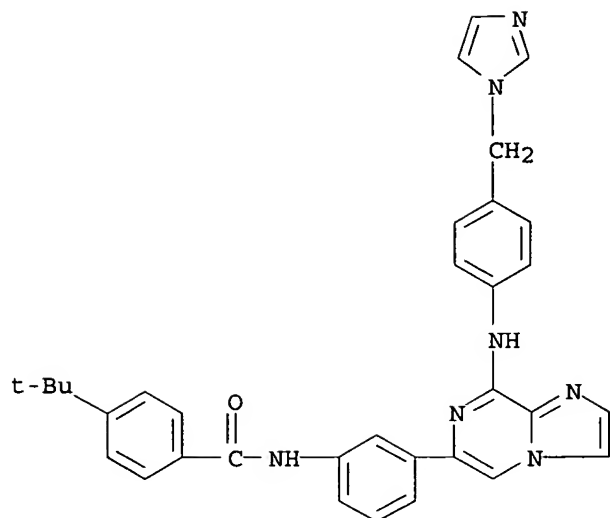
RN 845270-70-4 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(4-acetyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



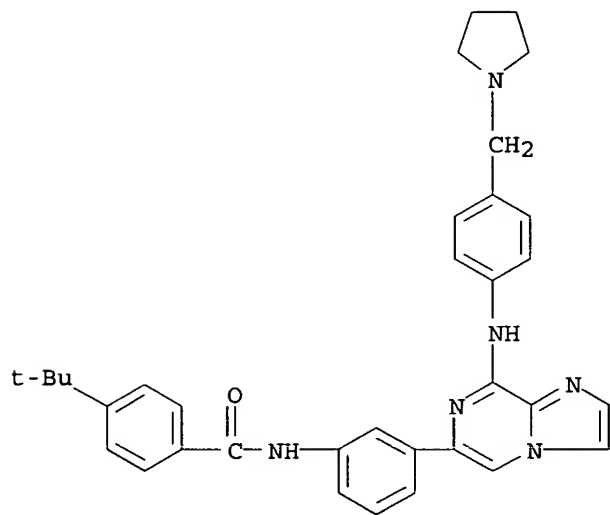
RN 845270-71-5 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1H-imidazol-1-ylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



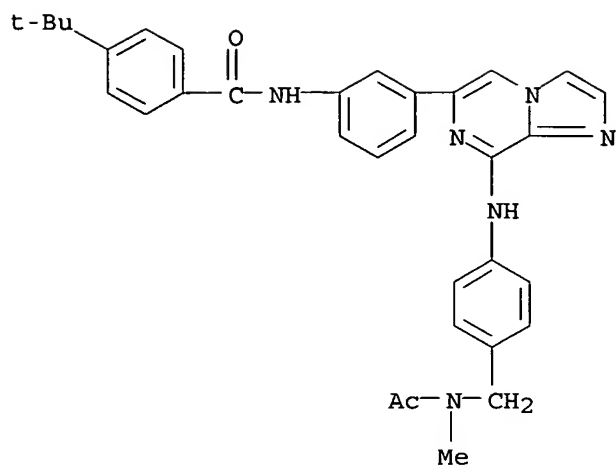
RN 845270-72-6 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-pyrrolidinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



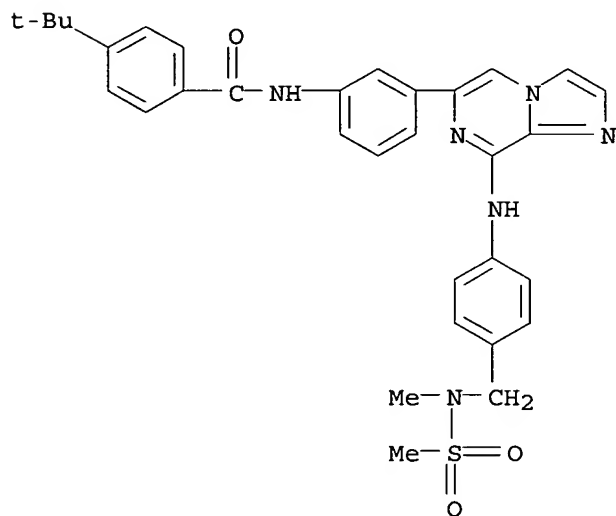
RN 845270-73-7 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(acetylmethylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



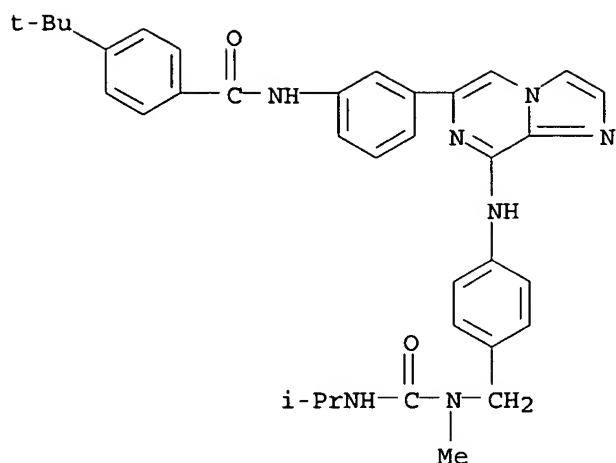
RN 845270-74-8 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[methyl(methylsulfonyl)amino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



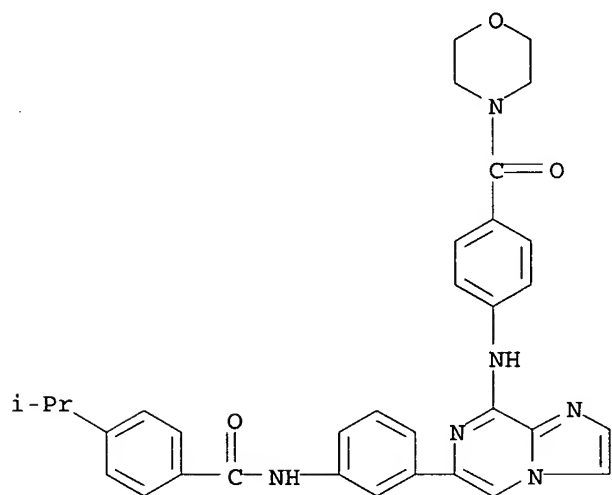
RN 845270-75-9 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[methyl[(1-methylethyl)amino]carbonyl]amino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



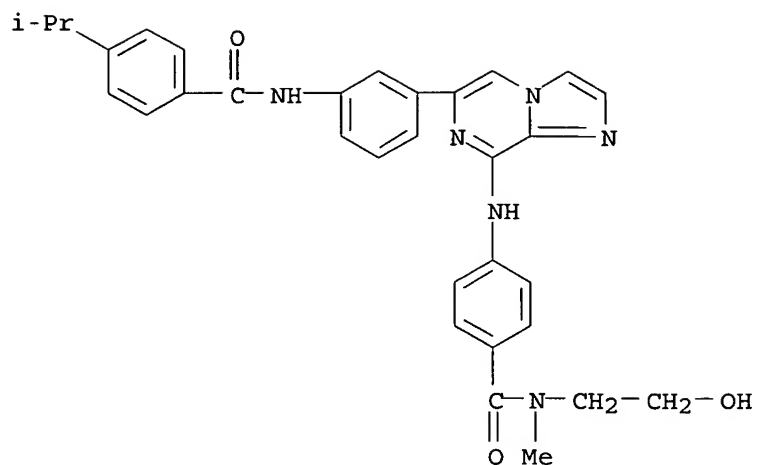
RN 845270-77-1 CAPLUS

CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



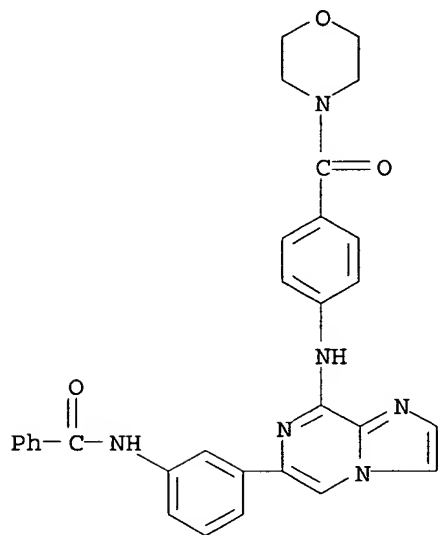
RN 845270-78-2 CAPLUS

CN Benzamide, N-(2-hydroxyethyl)-N-methyl-4-[[6-[3-[[4-(1-methylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino] - (9CI) (CA INDEX NAME)



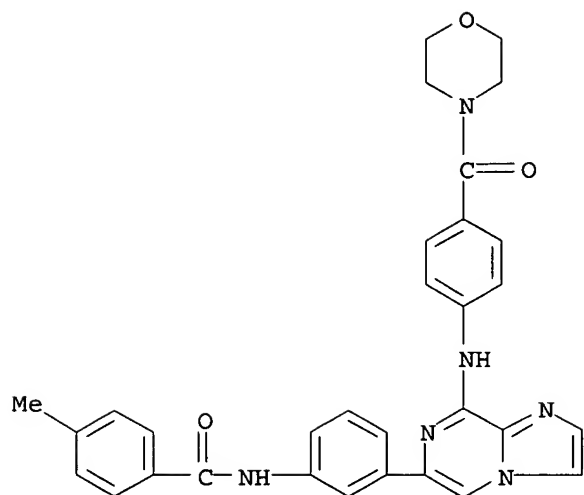
RN 845270-79-3 CAPLUS

CN Benzamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



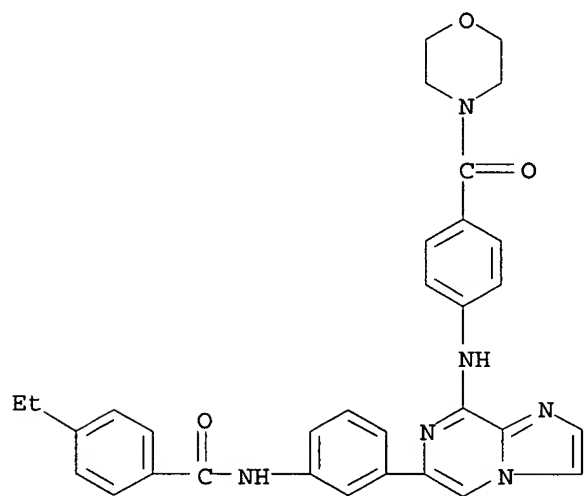
RN 845270-80-6 CAPLUS

CN Benzamide, 4-methyl-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



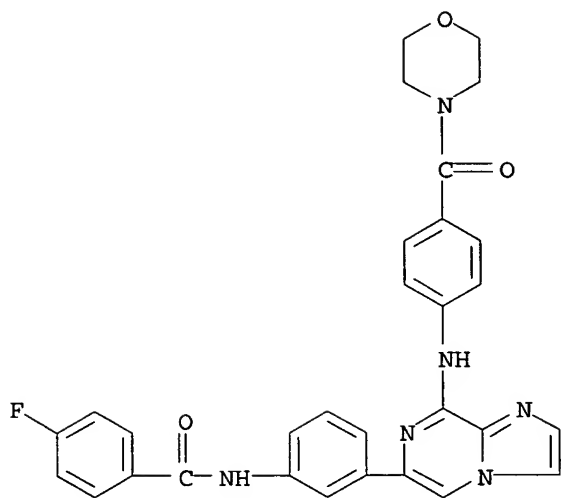
RN 845270-81-7 CAPLUS

CN Benzamide, 4-ethyl-N-[3-[8-[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo
[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



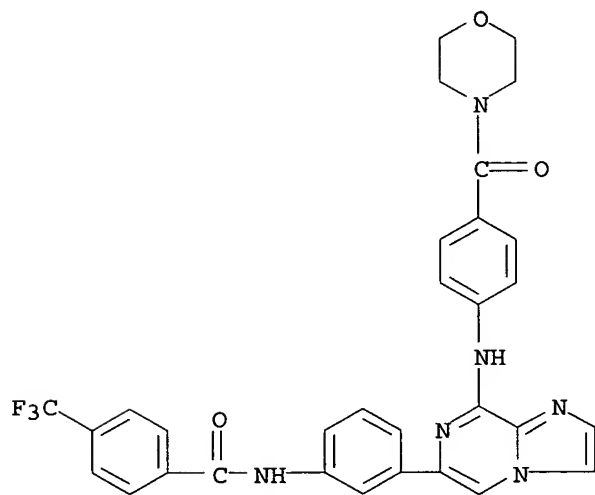
RN 845270-82-8 CAPLUS

CN Benzamide, 4-fluoro-N-[3-[8-[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo
[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



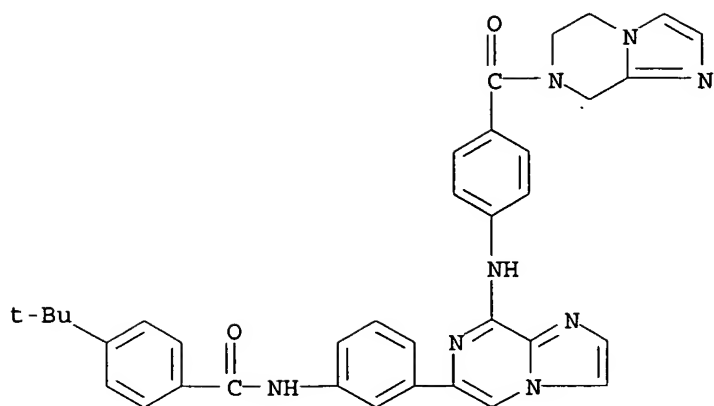
RN 845270-83-9 CAPLUS

CN Benzamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(trifluoromethyl) - (9CI) (CA INDEX NAME)



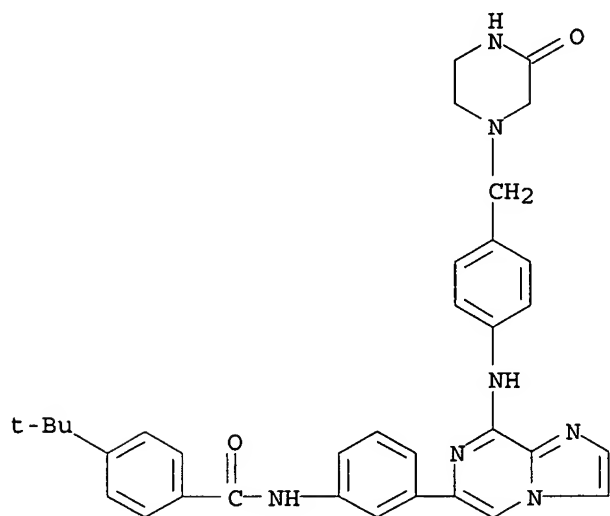
RN 845270-84-0 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl) - (9CI) (CA INDEX NAME)



RN 845270-85-1 CAPLUS

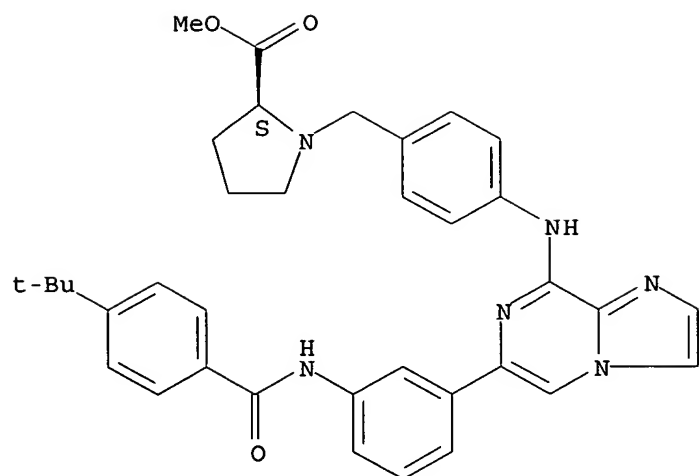
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



RN 845270-86-2 CAPLUS

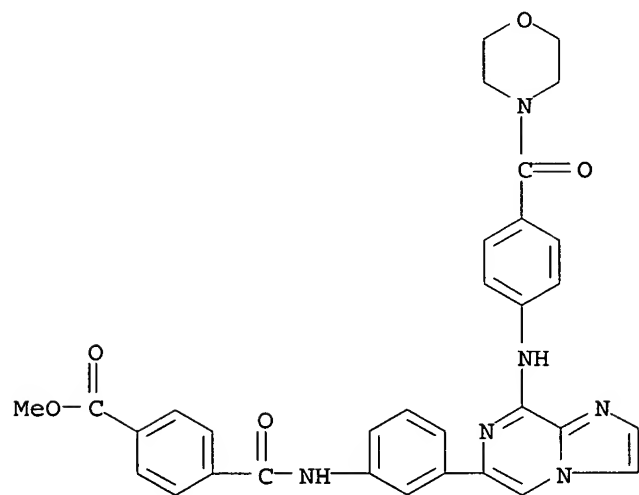
CN L-Proline, 1-[[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



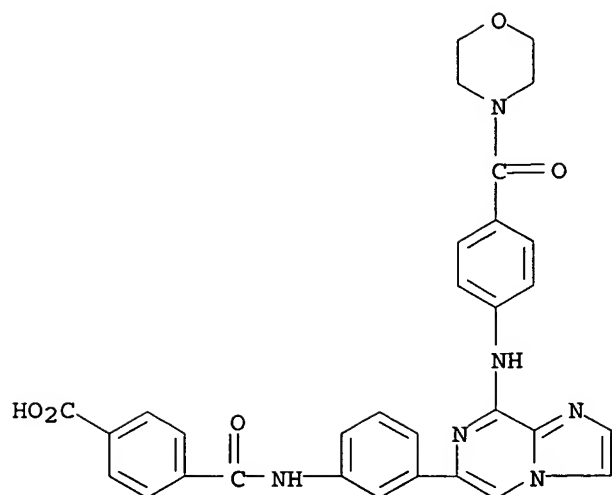
RN 845270-87-3 CAPLUS

CN Benzoic acid, 4-[[[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



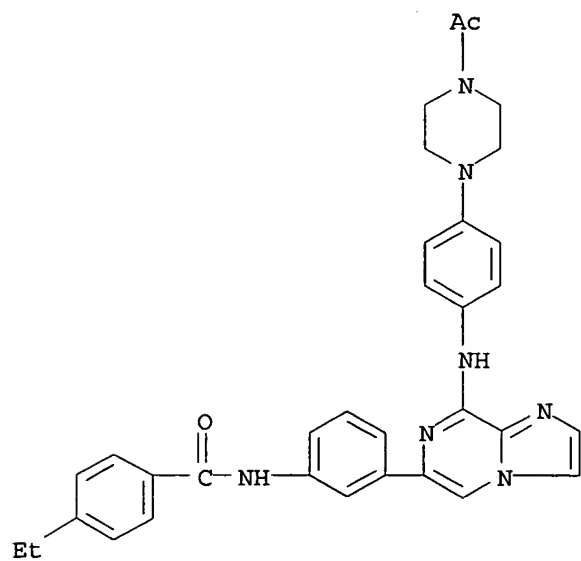
RN 845270-88-4 CAPLUS

CN Benzoic acid, 4-[[[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



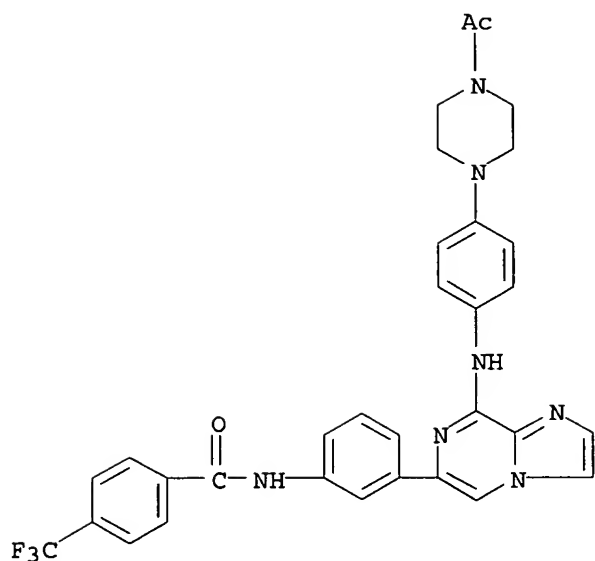
RN 845270-89-5 CAPLUS

CN Benzamide, N-[3-[8-[[4-(4-acetyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-ethyl- (9CI) (CA INDEX NAME)



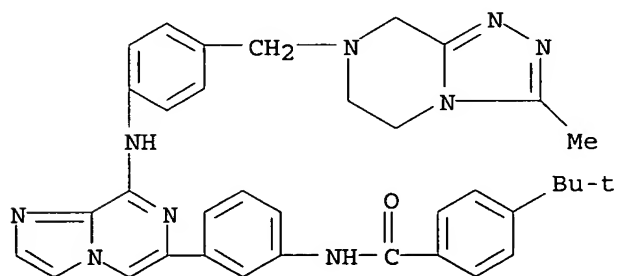
RN 845270-90-8 CAPLUS

CN Benzamide, N-[3-[8-[[4-(4-acetyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



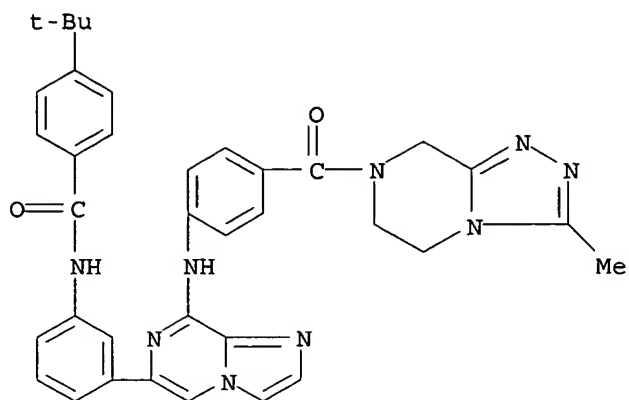
RN 845270-91-9 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(5,6-dihydro-3-methyl-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



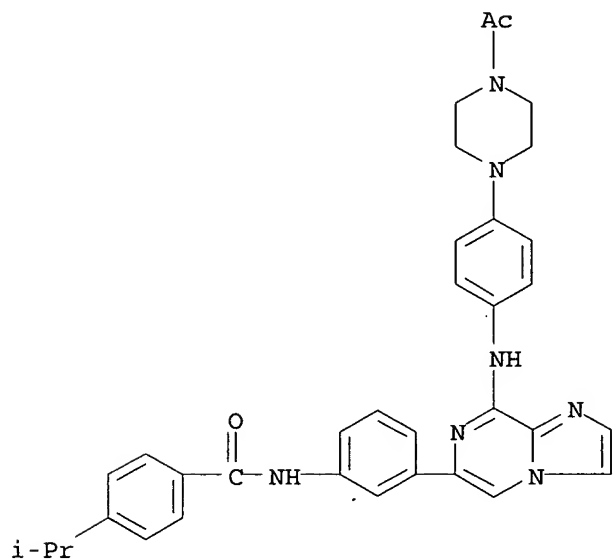
RN 845270-92-0 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(5,6-dihydro-3-methyl-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



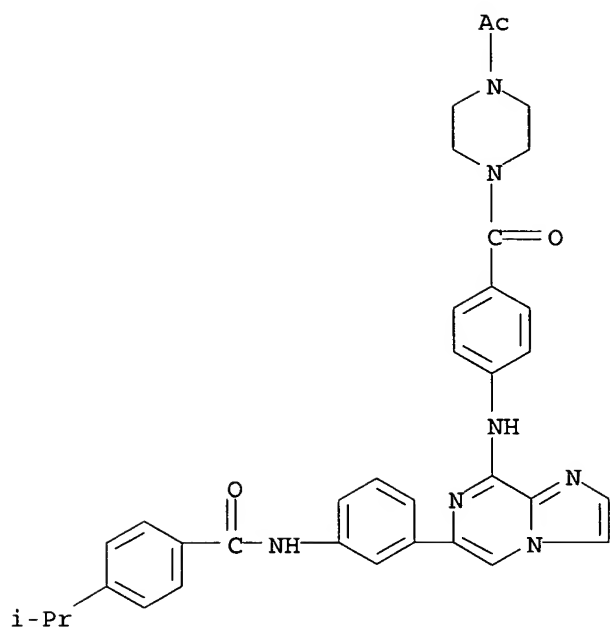
RN 845270-93-1 CAPLUS

CN Benzamide, N-[3-[8-[[4-(4-acetyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 845270-94-2 CAPLUS

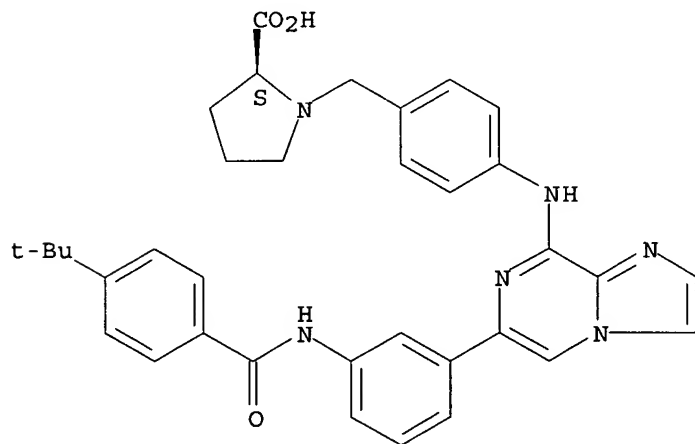
CN Benzamide, N-[3-[8-[[4-[(4-acetyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 845270-95-3 CAPLUS

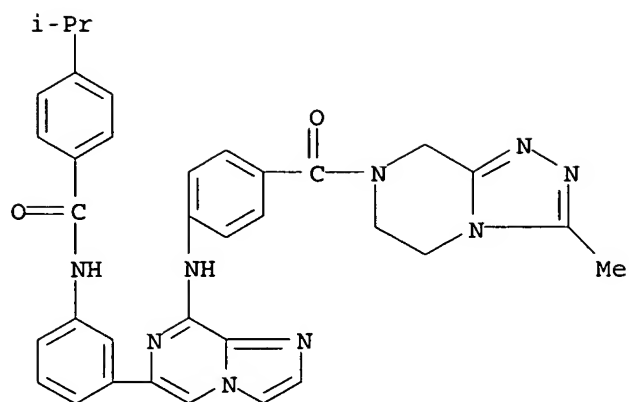
CN L-Proline, 1-[[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



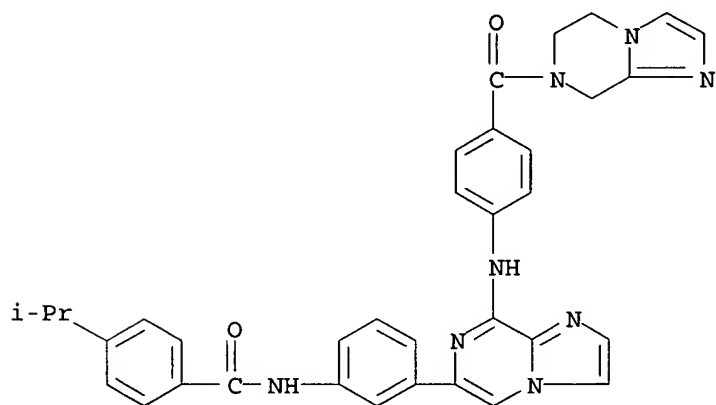
RN 845270-96-4 CAPLUS

CN Benzamide, N-[3-[8-[[4-[[5,6-dihydro-3-methyl-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



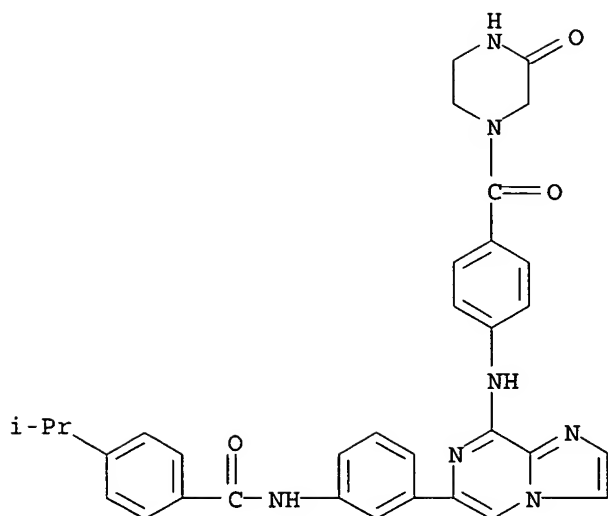
RN 845270-97-5 CAPLUS

CN Benzamide, N-[3-[8-[[4-[(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)-(9CI) (CA INDEX NAME)



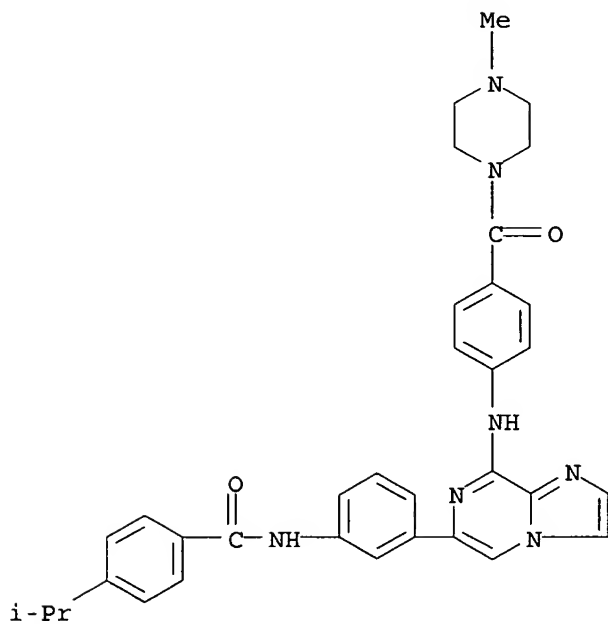
RN 845270-98-6 CAPLUS

CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



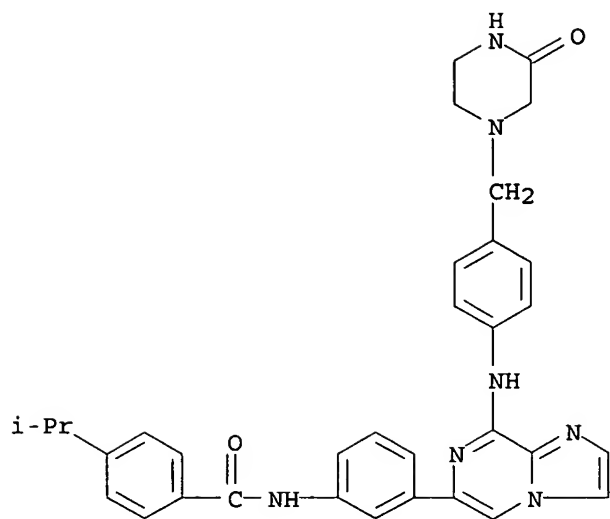
RN 845270-99-7 CAPLUS

CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-[(4-methyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



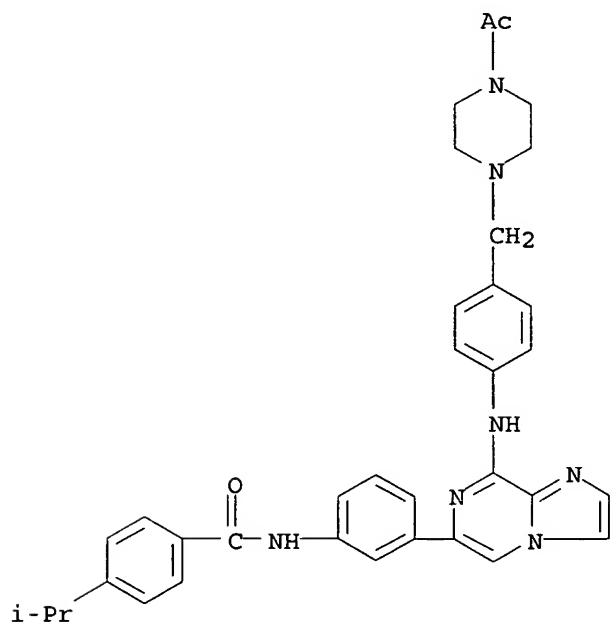
RN 845271-00-3 CAPLUS

CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



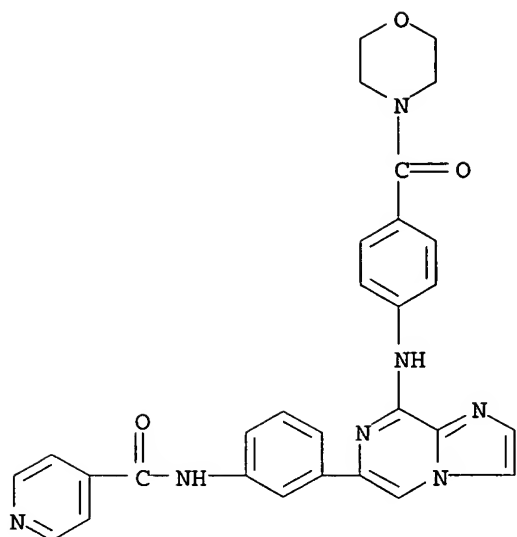
RN 845271-01-4 CAPLUS

CN Benzamide, N-[3-[8-[[4-(4-acetyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



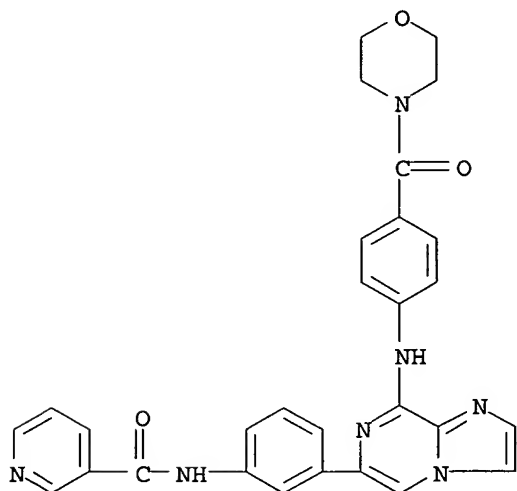
RN 845271-03-6 CAPLUS

CN 4-Pyridinecarboxamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



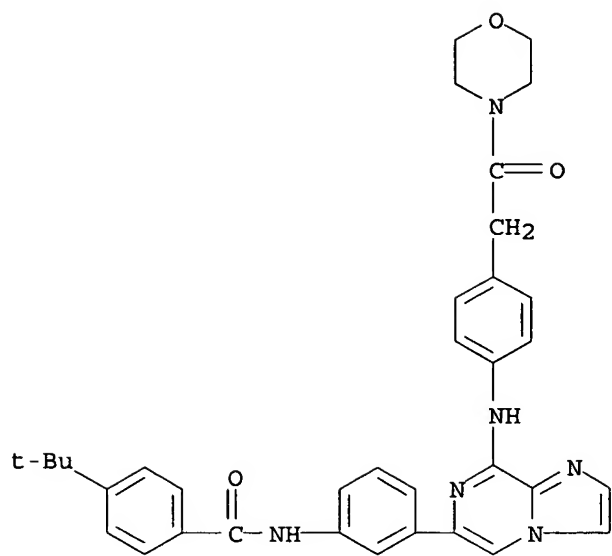
RN 845271-05-8 CAPLUS

CN 3-Pyridinecarboxamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



RN 845271-07-0 CAPLUS

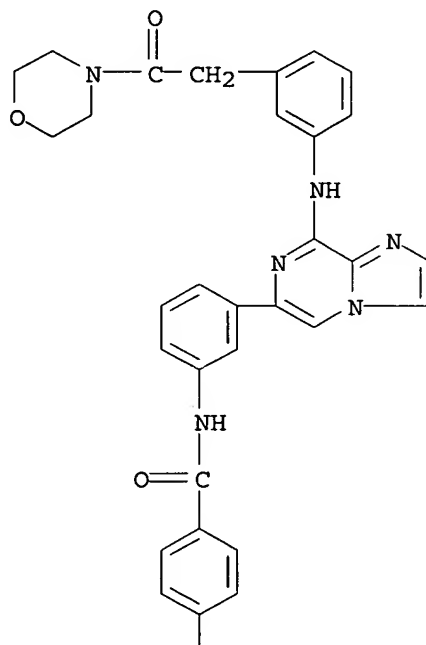
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-(4-morpholinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



RN 845271-09-2 CAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-[2-(4-morpholinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

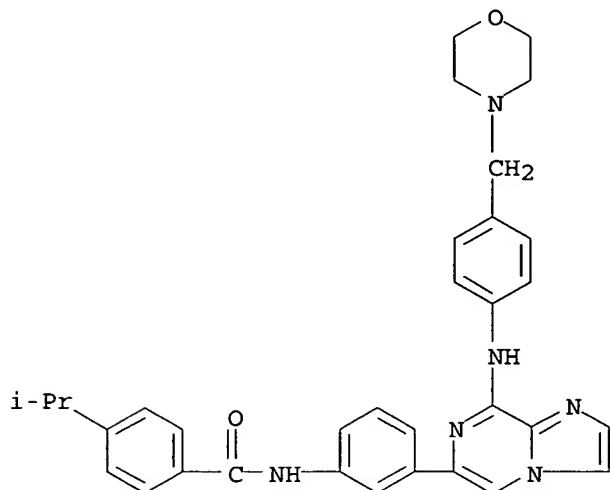
PAGE 1-A



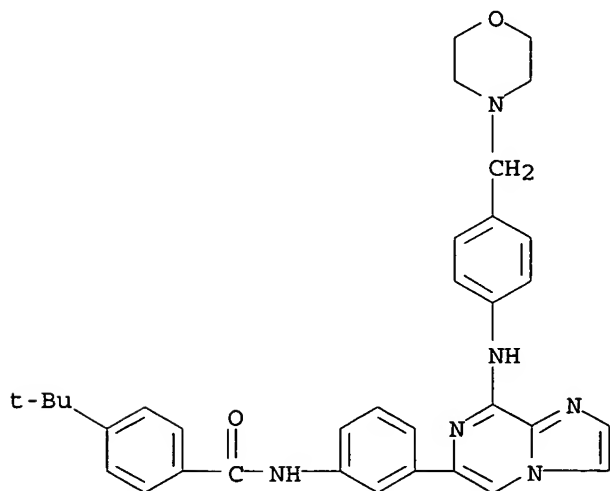
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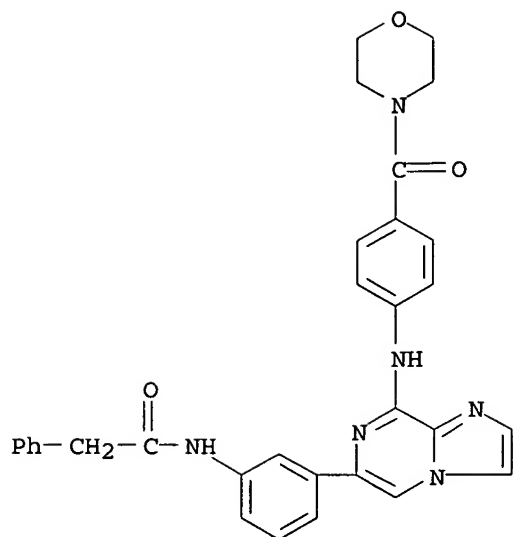
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 CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-(4-morpholinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845271-13-8 CAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-morpholinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

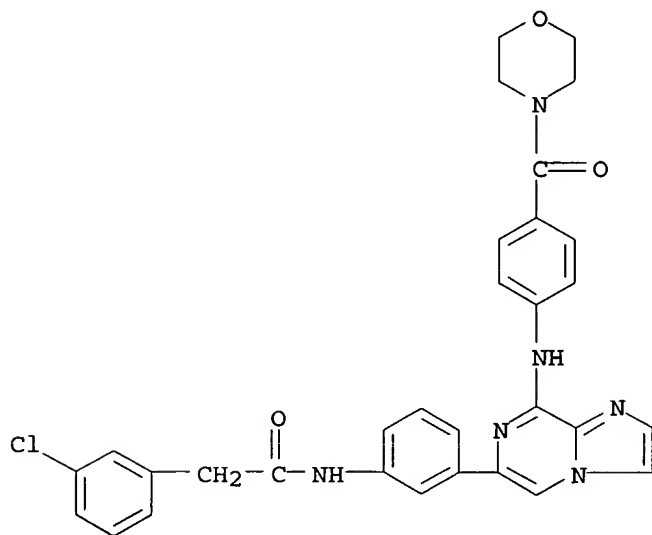


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 CN Benzeneacetamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



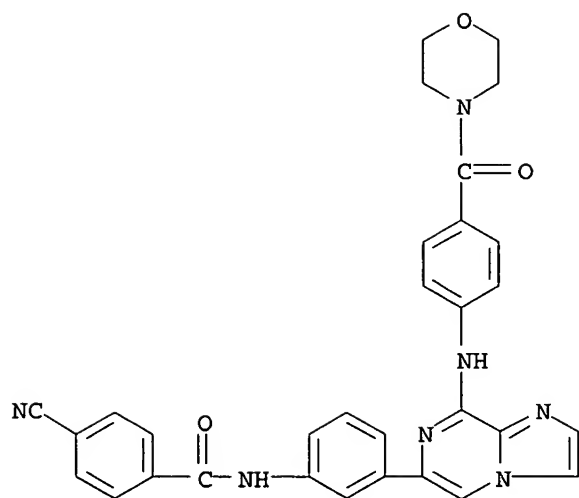
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CN Benzeneacetamide, 3-chloro-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



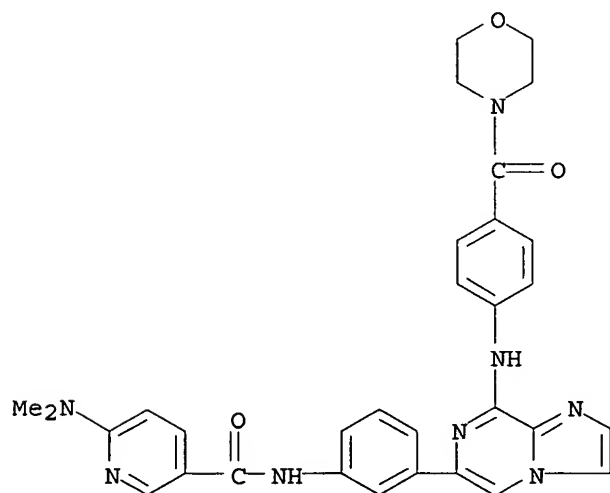
RN 845271-20-7 CAPLUS

CN Benzamide, 4-cyano-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



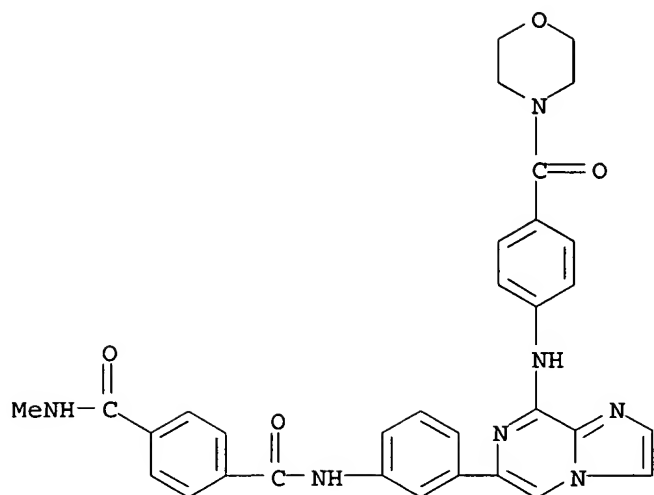
RN 845271-22-9 CAPLUS

CN 3-Pyridinecarboxamide, 6-(dimethylamino)-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



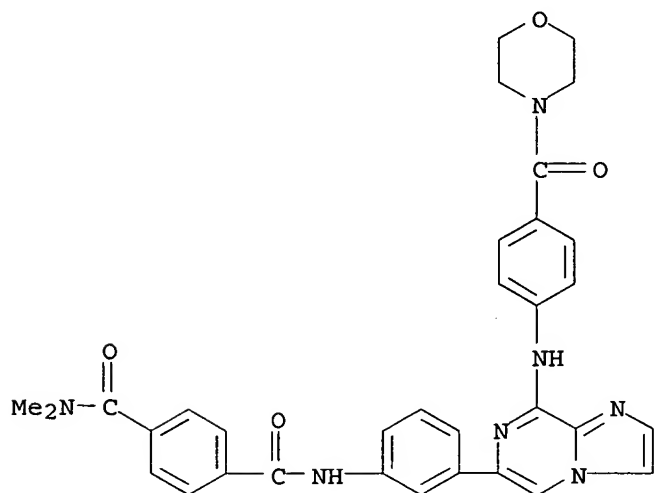
RN 845271-24-1 CAPLUS

CN 1,4-Benzenedicarboxamide, N-methyl-N'-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



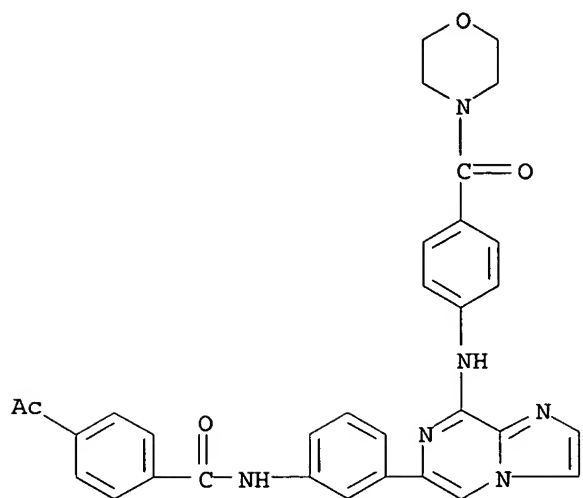
RN 845271-26-3 CAPLUS

CN 1,4-Benzenedicarboxamide, N,N-dimethyl-N'-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)

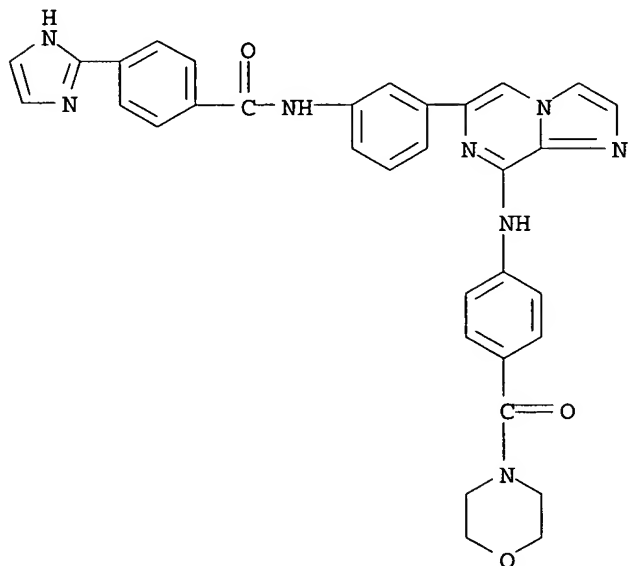


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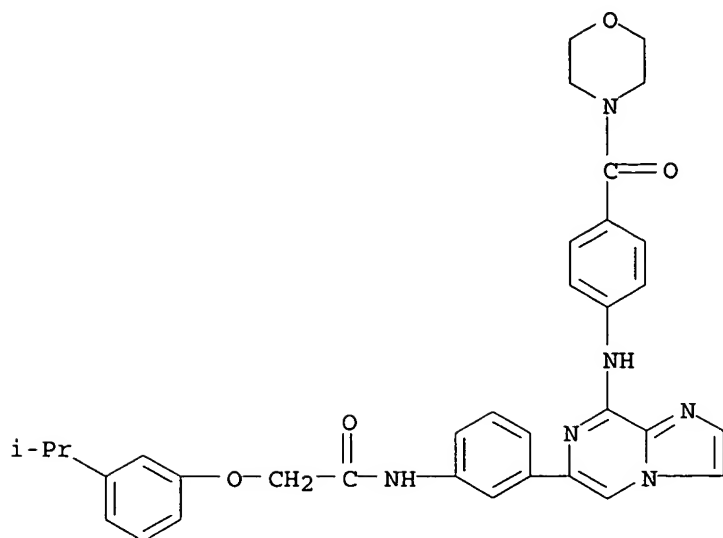
CN Benzamide, 4-acetyl-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845271-29-6 CAPLUS
 CN Benzamide, 4-(1H-imidazol-2-yl)-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
 (CA INDEX NAME)

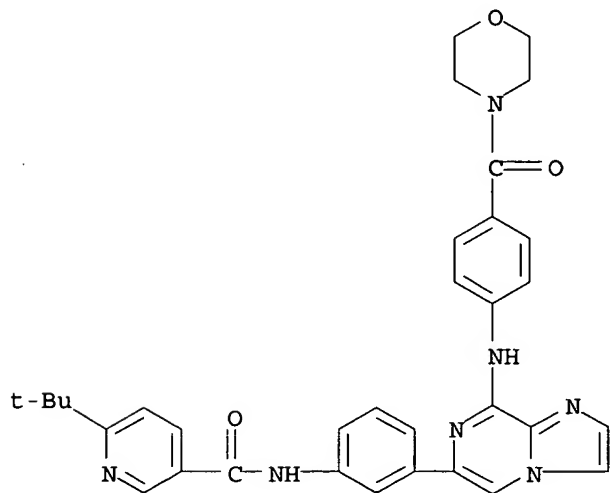


RN 845271-30-9 CAPLUS
 CN Acetamide, 2-[3-(1-methylethyl)phenoxy]-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
 (CA INDEX NAME)



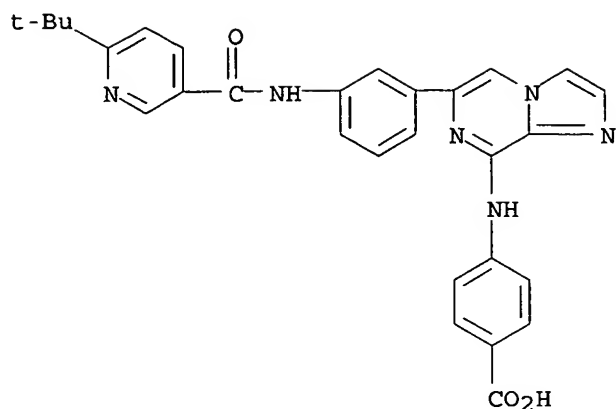
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CN 3-Pyridinecarboxamide, 6-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



RN 845271-34-3 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[[6-(1,1-dimethylethyl)-3-pyridinyl]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino] - (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:267339 CAPLUS

DOCUMENT NUMBER: 140:303700

TITLE: Preparation and pharmaceutical compositions of novel imidazopyrazines as cyclin dependent kinase inhibitors
INVENTOR(S): Paruch, Kamil; Guzi, Timothy J.; Dwyer, Michael P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Mallams, Alan K.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

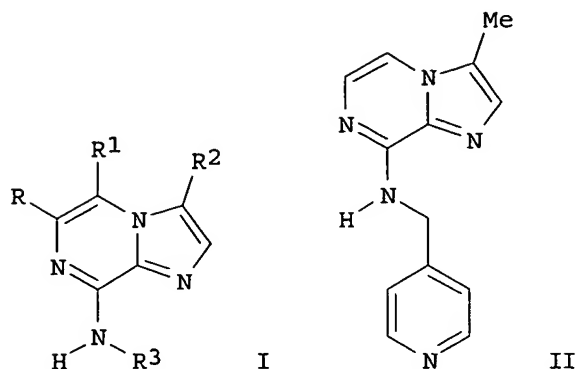
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026877	A1	20040401	WO 2003-US29209	20030919
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2499756	AA	20040401	CA 2003-2499756	20030919
AU 2003272476	A1	20040408	AU 2003-272476	20030919
EP 1543008	A1	20050622	EP 2003-754658	20030919
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1694886	A	20051109	CN 2003-825177	20030919
JP 2006507253	T2	20060302	JP 2004-537904	20030919
ZA 2005002375	A	20050927	ZA 2005-2375	20050322
PRIORITY APPLN. INFO.:			US 2002-412997P	P 20020923
			WO 2003-US29209	W 20030919

OTHER SOURCE(S): MARPAT 140:303700
 ED Entered STN: 01 Apr 2004
 GI



AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compds. of formula I [R = H, halo, (un)substituted-aryl, -heteroaryl, -cycloalkyl, etc.; R1 = H, halo or alkyl; R2 = halo, (un)substituted-alkyl, -aryl, -arylalkyl, etc.; R3 = H, (un)substituted-aryl, -heteroaryl, -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical

formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by condensation of 8-chloro-3-methylimidazo[1,2-a]pyrazine with 4-(aminomethyl)pyridine. I possessed excellent CDK inhibitory properties, e.g., II demonstrated an IC50 value of 22.5 μ M.

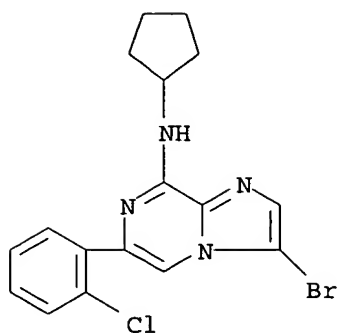
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 676360-39-7P 676360-41-1P 676360-43-3P
 676360-49-9P 676360-51-3P 676360-53-5P
 676360-55-7P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(drug candidate; combinatorial preparation of a library of imidazopyrazines as cyclin dependent kinase inhibitors)

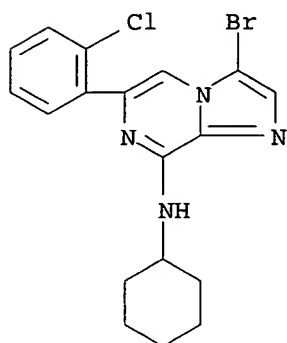
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CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-cyclopentyl-(9CI) (CA INDEX NAME)



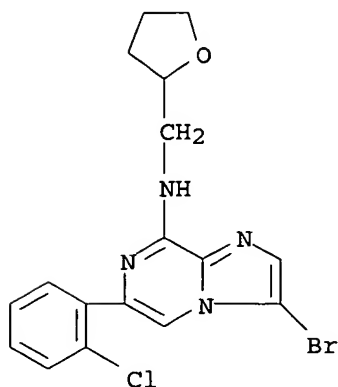
RN 676359-80-1 CAPLUS

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(9CI) (CA INDEX NAME)



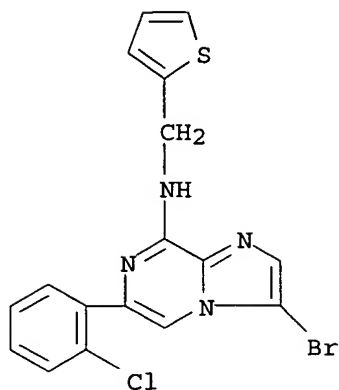
RN 676359-82-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



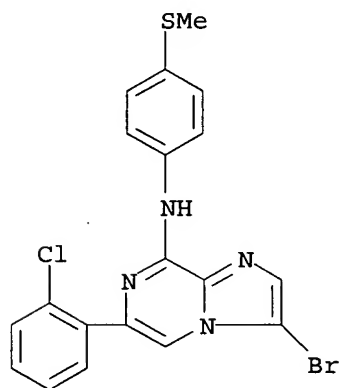
RN 676359-86-7 CAPLUS

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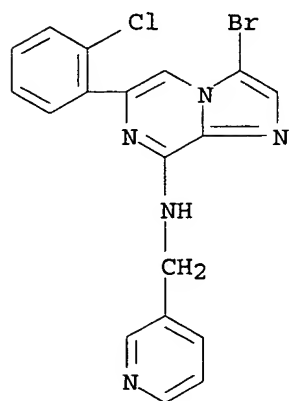
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CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[4-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



RN 676360-29-5 CAPLUS

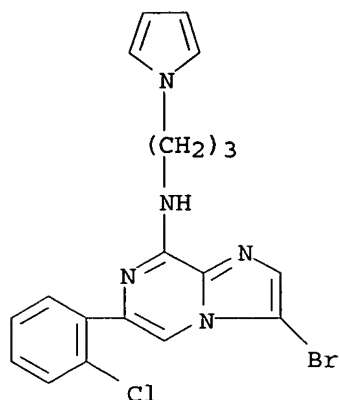
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RN 676360-33-1 CAPLUS

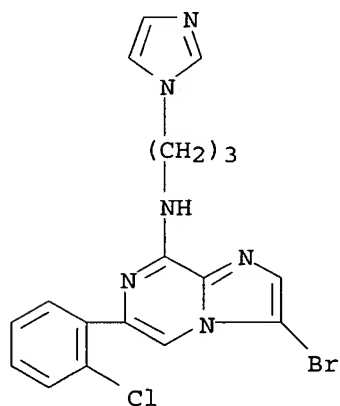
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1H-pyrrol-

1-yl)propyl]- (9CI) (CA INDEX NAME)



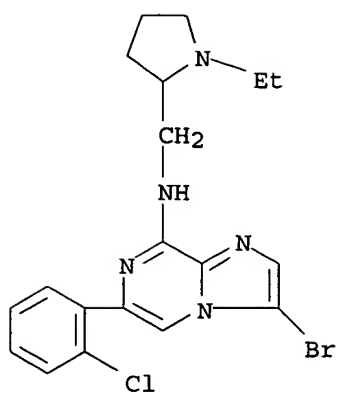
RN 676360-35-3 CAPLUS

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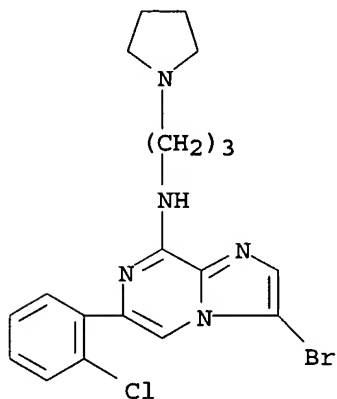
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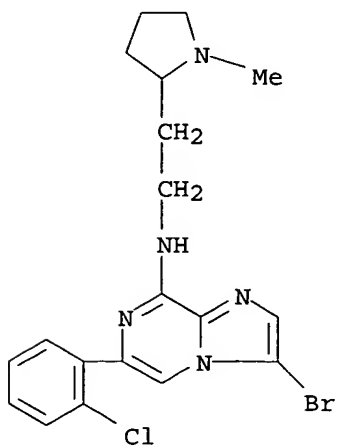
RN 676360-39-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)



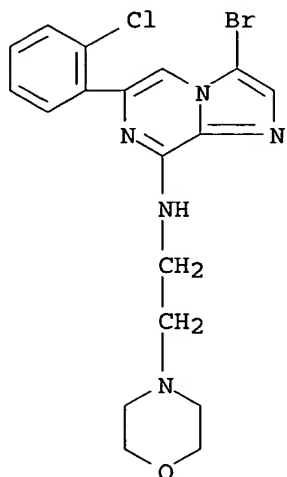
RN 676360-41-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



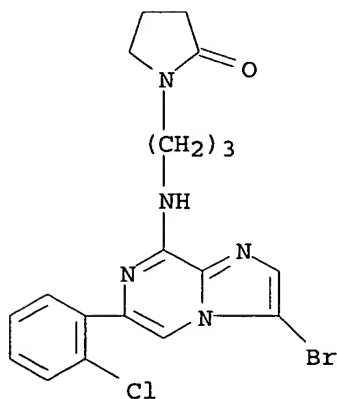
RN 676360-43-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



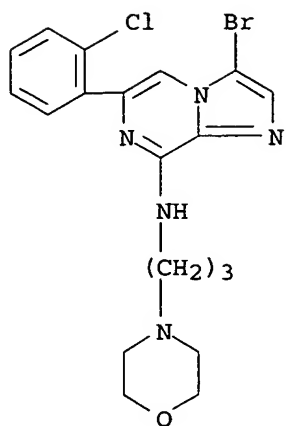
RN 676360-49-9 CAPLUS

CN 2-Pyrrolidinone, 1-[3-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]propyl]- (9CI) (CA INDEX NAME)



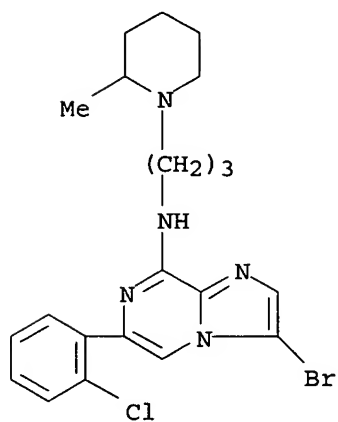
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CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



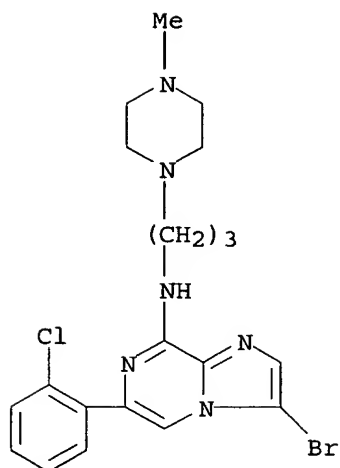
RN 676360-53-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(2-methyl-1-piperidiny)propyl]- (9CI) (CA INDEX NAME)



RN 676360-55-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)

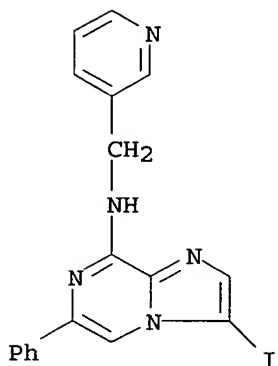


IT 676360-96-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of imidazopyrazines as cyclin dependent kinase inhibitors)

RN 676360-96-6 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-iodo-6-phenyl-N-(3-pyridinylmethyl)-
(9CI) (CA INDEX NAME)



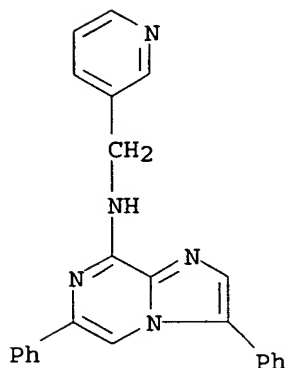
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676360-89-7P 676360-91-1P 676360-94-4P
676360-98-8P 676361-00-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

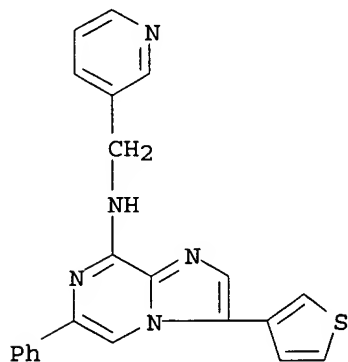
(drug candidate; preparation of imidazopyrazines as cyclin dependent kinase inhibitors)

RN 676359-47-0 CAPLUS

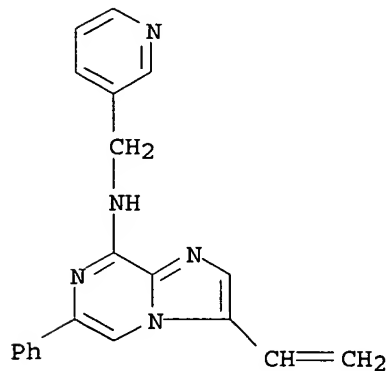
CN Imidazo[1,2-a]pyrazin-8-amine, 3,6-diphenyl-N-(3-pyridinylmethyl)- (9CI)
(CA INDEX NAME)



RN 676359-49-2 CAPLUS
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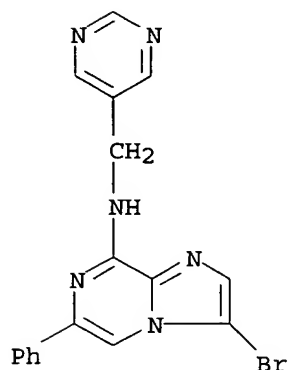


RN 676359-51-6 CAPLUS
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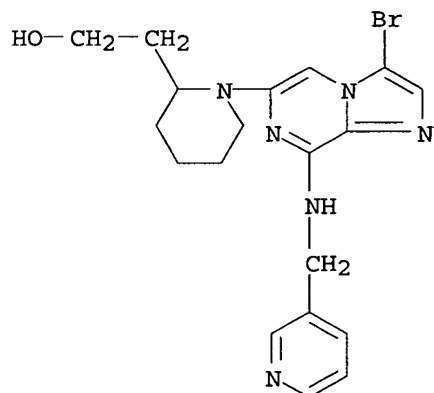
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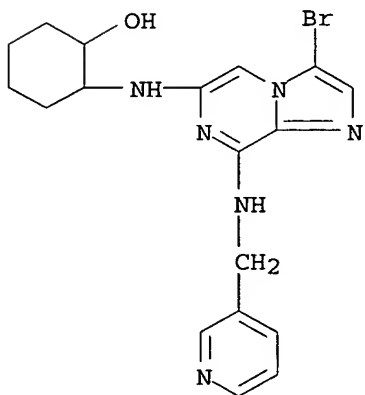
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CN 2-Piperidineethanol, 1-[3-bromo-8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



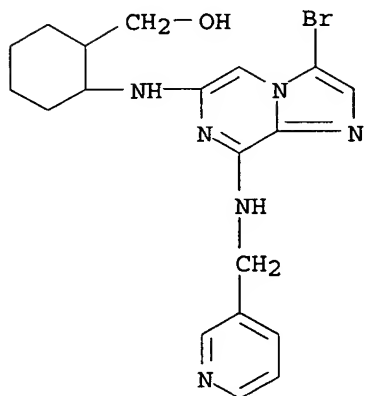
RN 676360-61-5 CAPLUS

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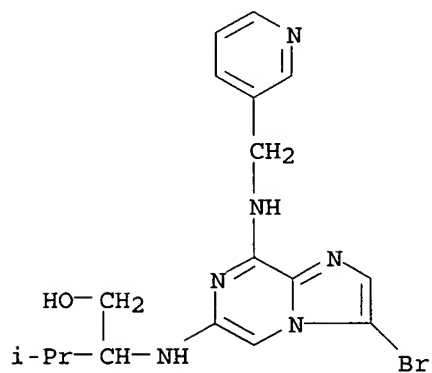
RN 676360-63-7 CAPLUS

CN Cyclohexanemethanol, 2-[[3-bromo-8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]amino] - (9CI) (CA INDEX NAME)



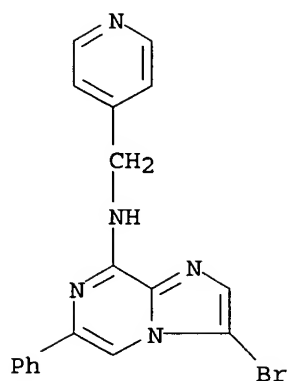
RN 676360-65-9 CAPLUS

CN 1-Butanol, 2-[[[3-bromo-8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]amino]-3-methyl- (9CI) (CA INDEX NAME)



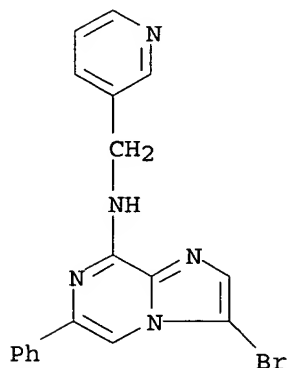
RN 676360-67-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(4-pyridinylmethyl) - (9CI) (CA INDEX NAME)



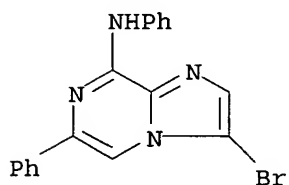
RN 676360-69-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(3-pyridinylmethyl)-
(9CI) (CA INDEX NAME)



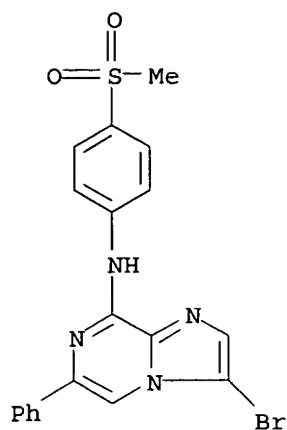
RN 676360-71-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N,6-diphenyl- (9CI) (CA INDEX
NAME)

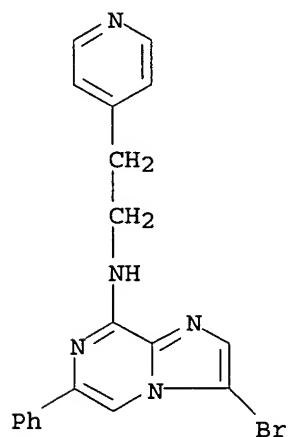


RN 676360-73-9 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N-[4-(methylsulfonyl)phenyl]-6-
phenyl- (9CI) (CA INDEX NAME)

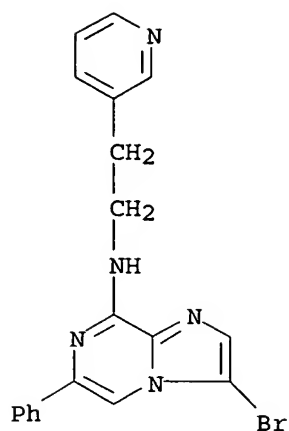


RN 676360-76-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[2-(4-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)

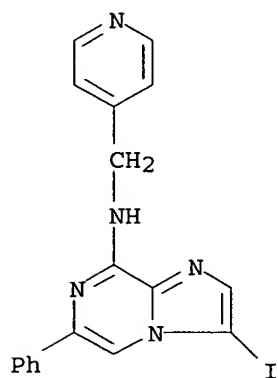
RN 676360-78-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[2-(3-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)



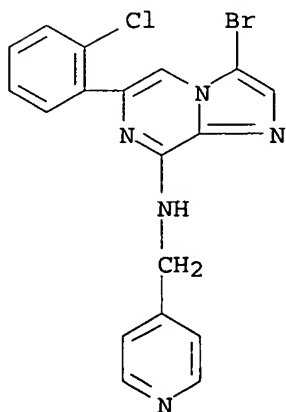
RN 676360-80-8 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-iodo-6-phenyl-N-(4-pyridinylmethyl) - (9CI) (CA INDEX NAME)



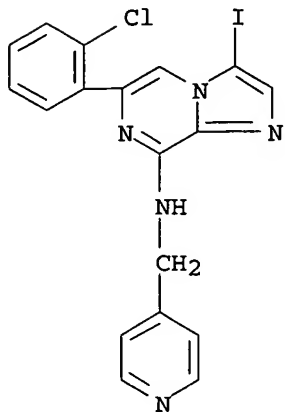
RN 676360-82-0 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(4-pyridinylmethyl) - (9CI) (CA INDEX NAME)



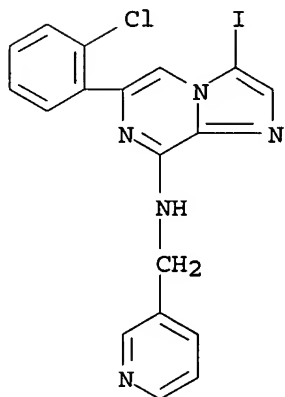
RN 676360-84-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-3-iodo-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



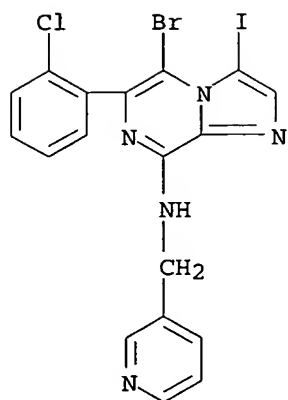
RN 676360-86-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-3-iodo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



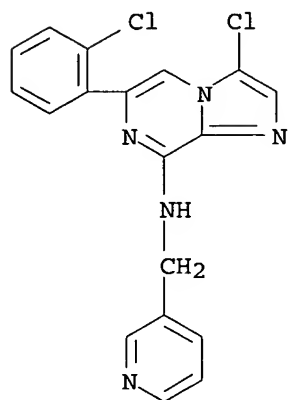
RN 676360-89-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 5-bromo-6-(2-chlorophenyl)-3-iodo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



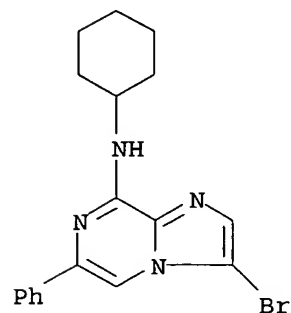
RN 676360-91-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-chloro-6-(2-chlorophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



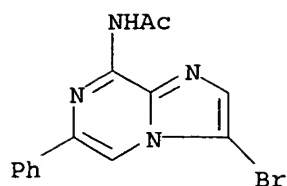
RN 676360-94-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N-cyclohexyl-6-phenyl- (9CI) (CA INDEX NAME)



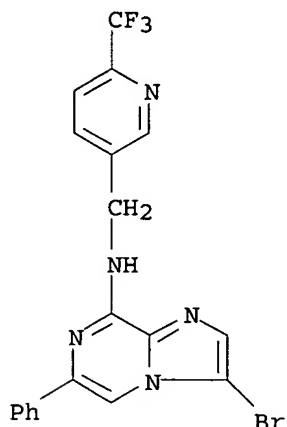
RN 676360-98-8 CAPLUS

CN Acetamide, N-(3-bromo-6-phenylimidazo[1,2-a]pyrazin-8-yl)- (9CI) (CA INDEX NAME)



RN 676361-00-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[[6-(trifluoromethyl)-3-pyridinyl]methyl]- (9CI) (CA INDEX NAME)



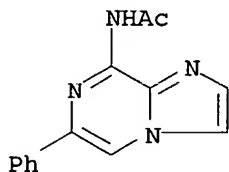
IT 676361-14-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of imidazopyrazines as cyclin dependent kinase inhibitors)

RN 676361-14-1 CAPLUS

CN Acetamide, N-(6-phenylimidazo[1,2-a]pyrazin-8-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:220337 CAPLUS

DOCUMENT NUMBER: 140:270878

TITLE: Kinase-modulating 6-aryl-imidazo[1,2-a]pyrazin-8-ylamines, method of their preparation, and method of their use, e.g., against cancer cells

INVENTOR(S): Desimone, Robert W.; Pippin, Douglas A.; Darrow, James W.; Mitchell, Scott A.; Currie, Kevin S.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA
 SOURCE: PCT Int. Appl., 74 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022562	A1	20040318	WO 2003-US28329	20030909
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003270489	A1	20040329	AU 2003-270489	20030909
US 2004067951	A1	20040408	US 2003-658121	20030909
PRIORITY APPLN. INFO.:			US 2002-409161P	P 20020909
			WO 2003-US28329	W 20030909

OTHER SOURCE(S): MARPAT 140:270878
 ED Entered STN: 19 Mar 2004
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, cycloalkylmethyl, (hetero)(cyclo)alkyl, sulfonamide, alkoxy, alkoxyalkoxy, alkoxyalkyl, (di)(alkyl)amino(alkyl), (un)substituted Ph or heteroaryl; R2 = (hetero)(cyclo)alkyl, cycloalkylmethyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, (di)(alkyl)amino(alkyl), (un)substituted Ph, heteroaryl, phenoxyphenyl, phenyl- or heteroarylpiperazine; R3 = H, CO₂H or esters, (hetero)(cyclo)alkyl, (un)substituted Ph, heteroaryl, phenoxyphenyl, phenyl- or heteroarylpiperazine; R4 = H, (hetero)(cyclo)alkyl, alkoxyalkyl, (un)substituted Ph, heteroaryl, phenoxyphenyl, phenyl- or heteroarylpiperazine; X = N or CH; Z1 = bond, CO, (un)substituted CH₂, CH₂CH₂, CONH; Z2 = bond, CO, (un)substituted CH₂NHCONH, NHCONHCH₂, CH₂, CH₂CH₂, CONH, NHCO, NHCONH, SO₂NH, NHSO₂; some substituents may be linked; with provisos] and their pharmaceutically acceptable salts, hydrates, solvates, crystal forms, diastereomers, prodrugs, or mixts., are disclosed. Compds. I are of particular utility in the treatment of kinase-implicated disorders. A list of 91 invention compds. is given in examples, and the compds. are individually claimed. A general preparatory method starting from 3,5-dibromo-2-aminopyrazine is given; the steps include (among others) cyclocondensation with α -bromo aldehydes, monoaminolysis of the resultant 6,8-dibromoimidazopyrazines, Pd-catalyzed arylation of the obtained 8-amino-6-bromoimidazopyrazines, and reaction of 6-(aminophenyl)imidazolpyrazines with Ph isocyanate derivs. to form ureas. An exemplary invention compound is II. In tests against human cancer cell lines, including one over-expressing transfected human myrAKT-1 kinase gene (AKT-1 kinase), exemplified compds. I had IC₅₀ values \leq 25 μ M.

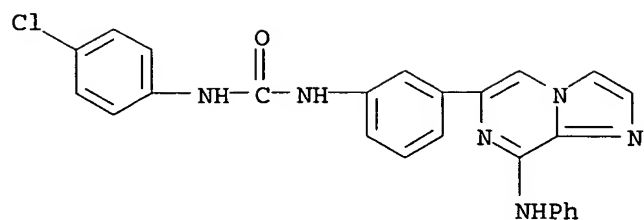
IT 618454-80-1P, 1-(4-Chlorophenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]urea 618454-86-7P, 1-(4-Chlorophenyl)-3-[3-[8-(4-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 618454-91-4P, 1-(4-Chlorophenyl)-3-[3-[8-(3-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 618455-30-4P, 4-[6-[3-[3-(4-Chlorophenyl)ureido]phenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid ethyl ester 618455-73-5P, 4-[6-[4-(Piperidine-1-carbonyl)phenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid ethyl ester 618455-75-7P, 4-[6-[3-[3-(2-Methylsulfanylphenyl)ureido]phenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid ethyl ester 618455-77-9P, [4-[8-(4-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]piperidin-1-ylmethanone 618455-84-8P, 1-(3-Chloro-4-fluorophenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]urea 618455-86-0P, 1-[3-(8-Phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]-3-(3-trifluoromethylphenyl)urea 618455-88-2P, 1-(2-Chloro-5-trifluoromethylphenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]urea 618455-91-7P, 1-[3-[8-(4-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea 618455-94-0P, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(3-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 618455-97-3P, 1-[3-[8-(3-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea 618455-99-5P, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(2-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 673857-11-9P, 1-[3-(8-Phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]-3-(4-trifluoromethylphenyl)urea 673857-12-0P, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[(pyridin-2-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 673857-13-1P, 1-(4-Chlorophenyl)-3-[3-[8-[(pyridin-3-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 673857-14-2P, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[(pyridin-3-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 673857-15-3P, 1-(4-Chlorophenyl)-3-[3-[8-[(pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 673857-16-4P, 1-[3-[8-[(Pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea 673857-17-5P, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[(pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 673857-20-0P, 1-(4-Chlorophenyl)-3-[3-[8-[(pyridin-2-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea 673857-21-1P, 1-[3-[8-[(Pyridin-2-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea 673857-23-3P, 1-(2-Methoxy-5-methylphenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]urea 673857-24-4P, 1-[3-[8-(3-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methoxy-5-methylphenyl)urea 673857-25-5P, 1-[3-[8-(2-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methoxy-5-methylphenyl)urea

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of arylimidazopyrazinylamines as kinase modulators)

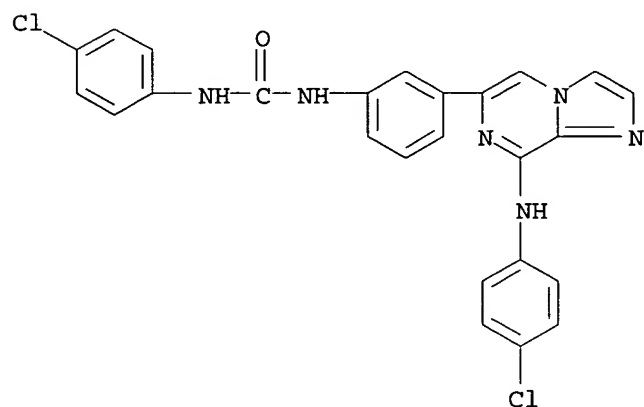
RN 618454-80-1 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



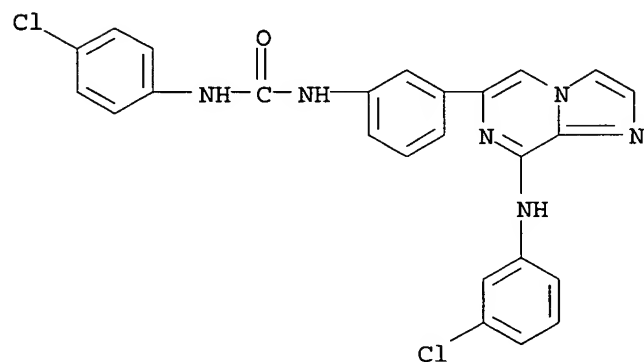
RN 618454-86-7 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



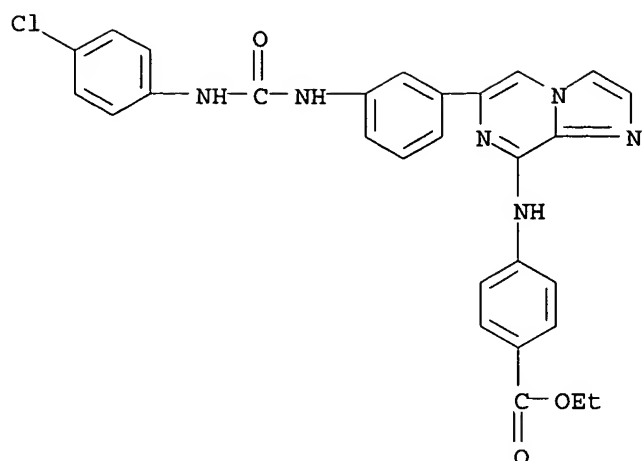
RN 618454-91-4 CAPLUS

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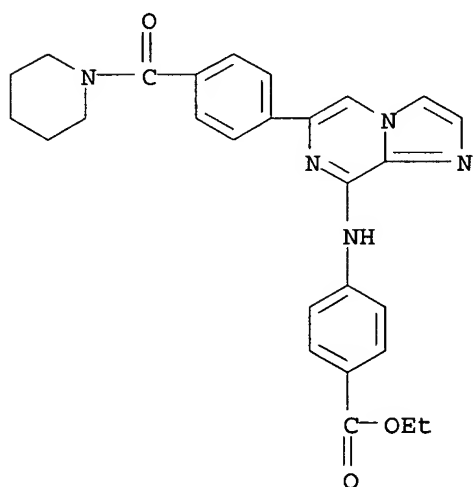
RN 618455-30-4 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[[(4-chlorophenyl)amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



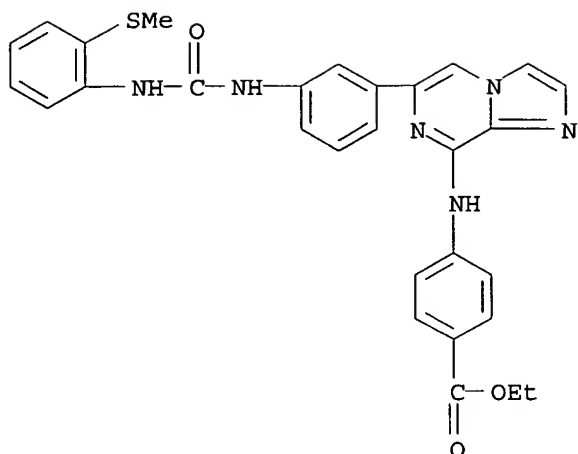
RN 618455-73-5 CAPLUS

CN Benzoic acid, 4-[[6-[4-(1-piperidinylcarbonyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



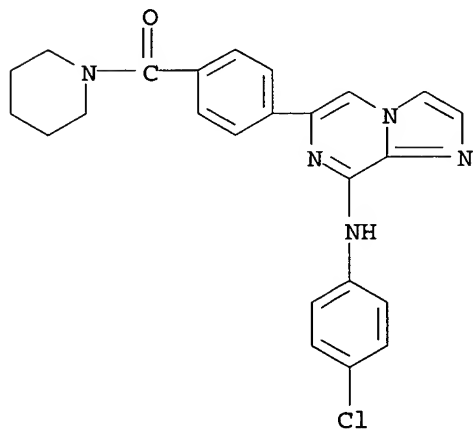
RN 618455-75-7 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[[2-(methylthio)phenyl]amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



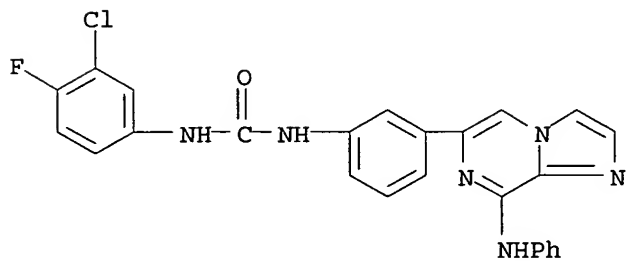
RN 618455-77-9 CAPLUS

CN Piperidine, 1-[4-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



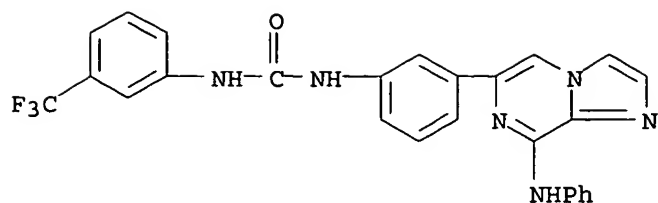
RN 618455-84-8 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



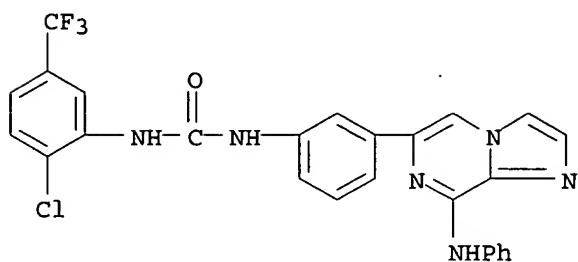
RN 618455-86-0 CAPLUS

CN Urea, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



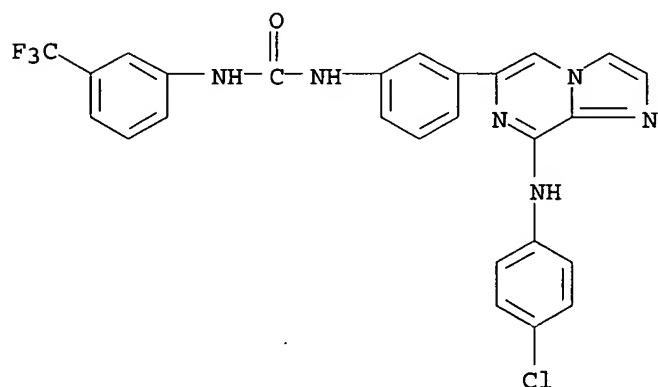
RN 618455-88-2 CAPLUS

CN Urea, N-[2-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



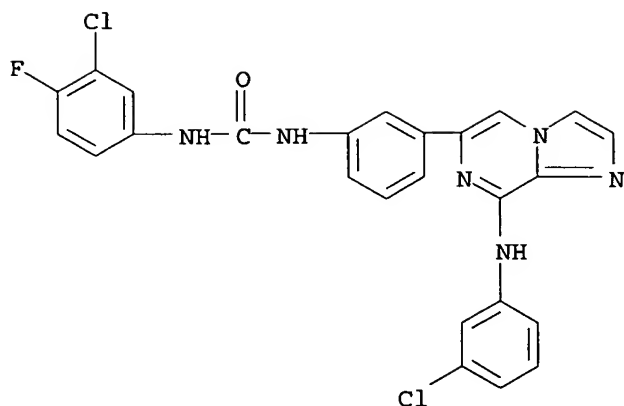
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CN Urea, N-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



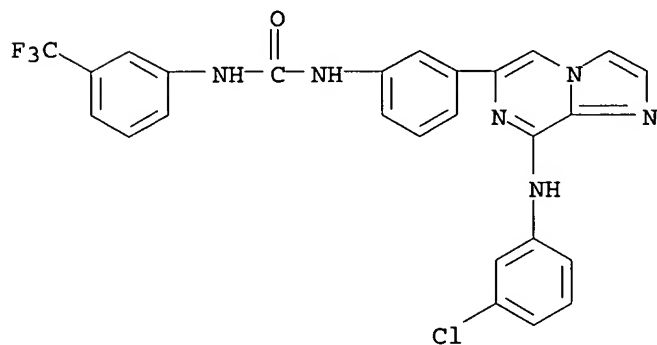
RN 618455-94-0 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



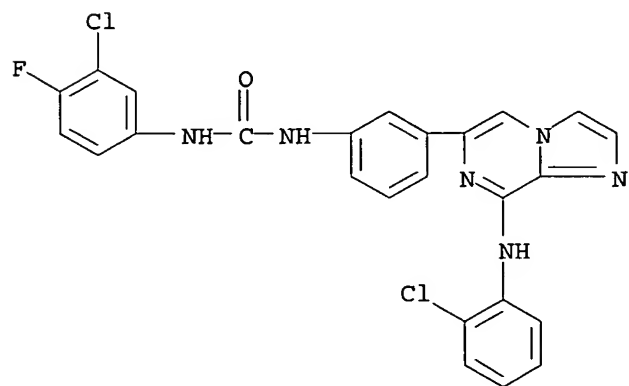
RN 618455-97-3 CAPLUS

CN Urea, N-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 618455-99-5 CAPLUS

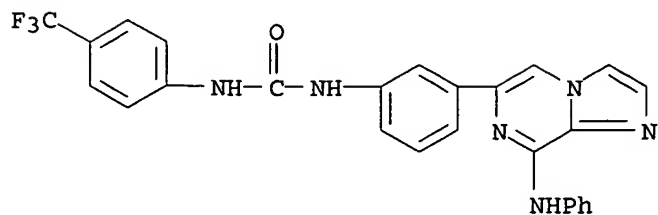
CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 673857-11-9 CAPLUS

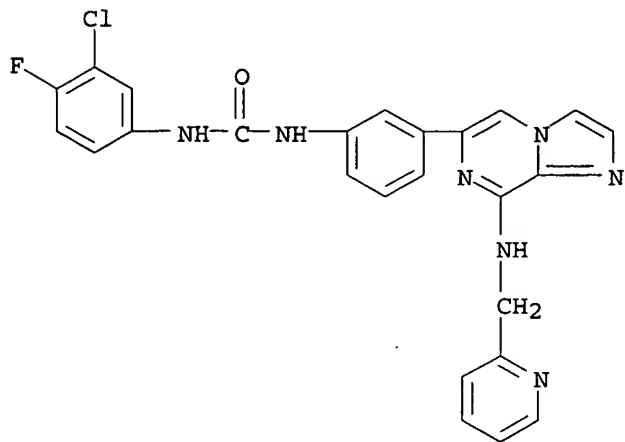
CN Urea, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-(3-chlorophenyl)phenyl]-

(trifluoromethyl)phenyl] - (9CI) (CA INDEX NAME)



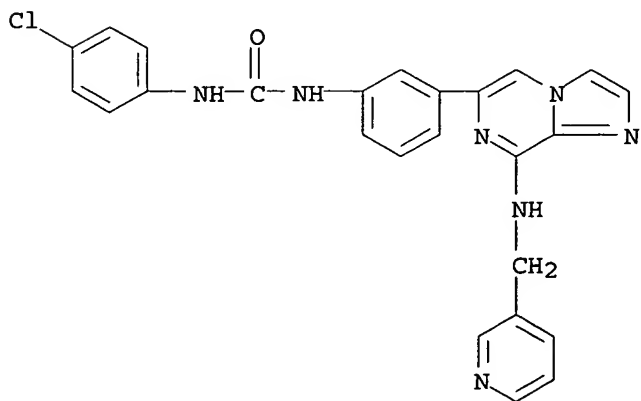
RN 673857-12-0 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(2-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



RN 673857-13-1 CAPLUS

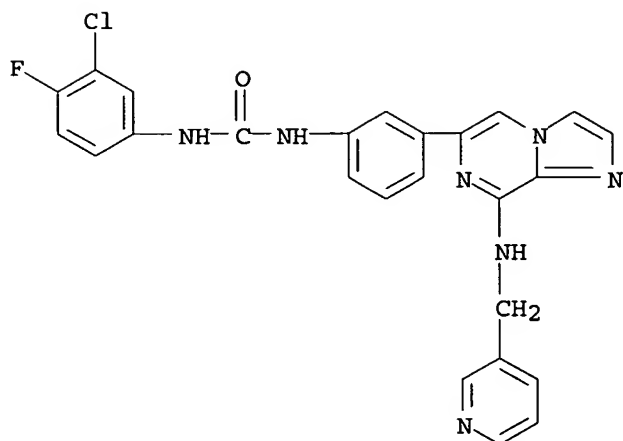
CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



RN 673857-14-2 CAPLUS

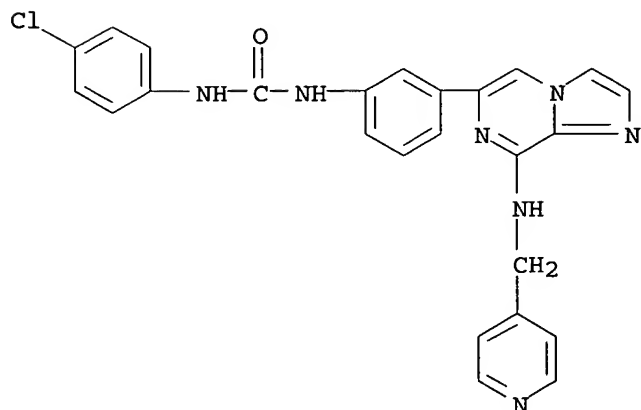
CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)

pyridinylmethyl) amino] imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



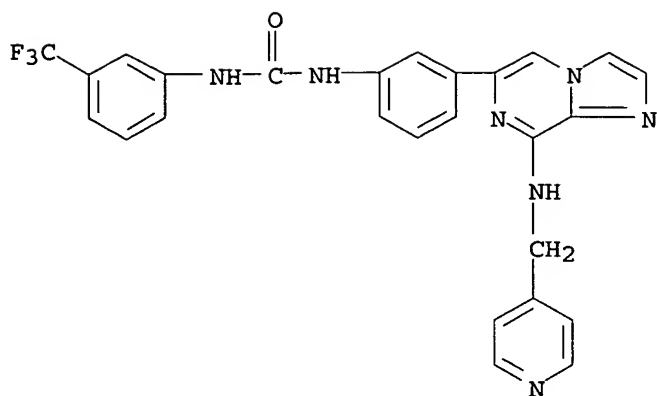
RN 673857-15-3 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(4-pyridinylmethyl) amino] imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



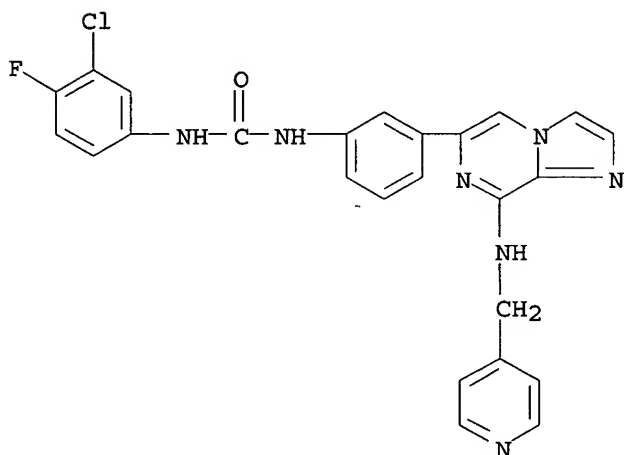
RN 673857-16-4 CAPLUS

CN Urea, N-[3-[8-[(4-pyridinylmethyl) amino] imidazo[1,2-a]pyrazin-6-yl]phenyl] - N'-[3-(trifluoromethyl)phenyl] - (9CI) (CA INDEX NAME)



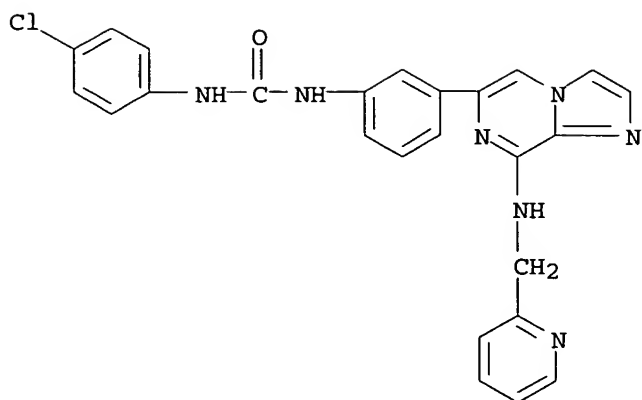
RN 673857-17-5 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



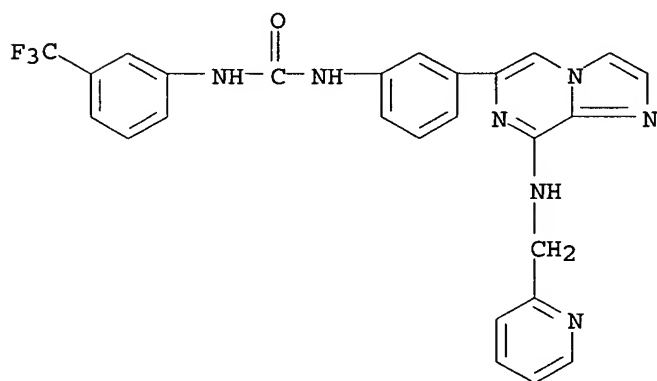
RN 673857-20-0 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(2-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



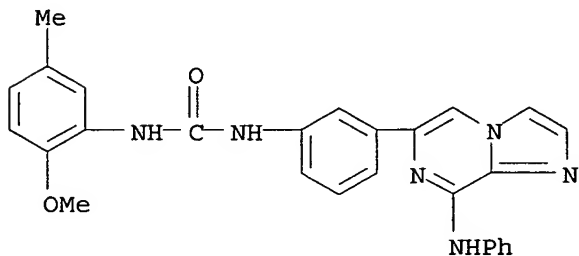
RN 673857-21-1 CAPLUS

CN Urea, N-[3-[8-[(2-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(3-(chloromethyl)phenyl)- (9CI) (CA INDEX NAME)



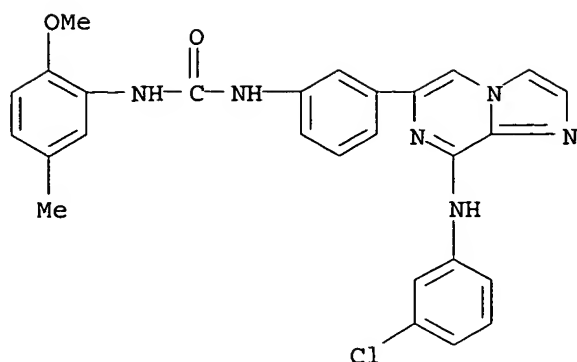
RN 673857-23-3 CAPLUS

CN Urea, N-(2-methoxy-5-methylphenyl)-N'-(3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl)- (9CI) (CA INDEX NAME)



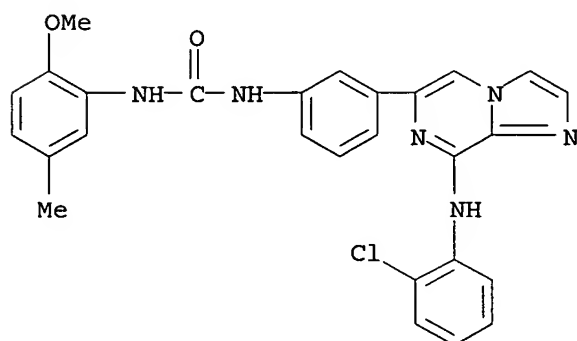
RN 673857-24-4 CAPLUS

CN Urea, N-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methoxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



RN 673857-25-5 CAPLUS

CN Urea, N-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methoxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:855931 CAPLUS

DOCUMENT NUMBER: 139:350757

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines as AKT-1 kinase inhibitors

INVENTOR(S): Desimone, Robert Walter, Jr.; Pippin, Douglas A.; Darrow, James W.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089434	A2	20031030	WO 2003-US12222	20030421
WO 2003089434	A3	20040115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
 TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2482991	AA	20031030	CA 2003-2482991	20030421
AU 2003221731	A1	20031103	AU 2003-221731	20030421
US 2003212073	A1	20031113	US 2003-419682	20030421
US 6919340	B2	20050719		
BR 2003009398	A	20050201	BR 2003-9398	20030421
EP 1509526	A2	20050302	EP 2003-718470	20030421

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN 1668619	A	20050914	CN 2003-814467	20030421
JP 2005530739	T2	20051013	JP 2003-586154	20030421
NO 2004004974	A	20041116	NO 2004-4974	20041116

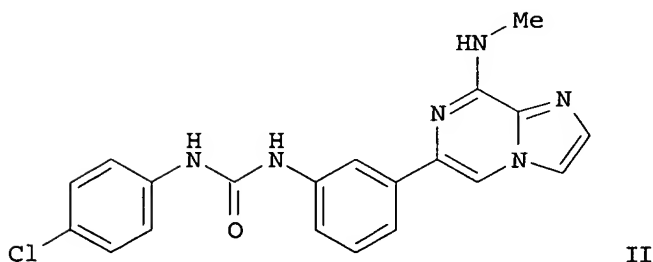
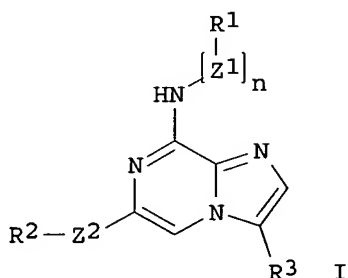
PRIORITY APPLN. INFO.:

US 2002-374213P	P	20020419
WO 2003-US12222	W	20030421

OTHER SOURCE(S): MARPAT 139:350757

ED Entered STN: 31 Oct 2003

GI



AB The title compds. [I; R1 = H, cycloalkylmethyl, alkyl, etc.; R2 = alkyl, cycloalkylmethyl, alkoxy, etc.; R3 = H, alkyl, etc.; Z1 = CO, (un)substituted (CH2)_m, CONH, NHSO₂, SO₂NH; n = 0-1; m = 0-2; Z2 = phenylene, naphthylene, CO, etc.] which are of particular utility in the treatment of kinase-implicated disorders, were prepared. General methods of preparation were given. All exemplified compds. I such as II were tested in standard AKT-1 kinase assay and standard assay to evaluate modulation of cell growth in soft agar (using cell lines HCT-15, MiaPaca2, MCF-7 and NIH3T3 clone stably overexpressing transfected myrAkt-1 human gene), and exhibited IC₅₀ of ≤ 25 μM. Pharmaceutical composition comprising the

compound I is claimed.

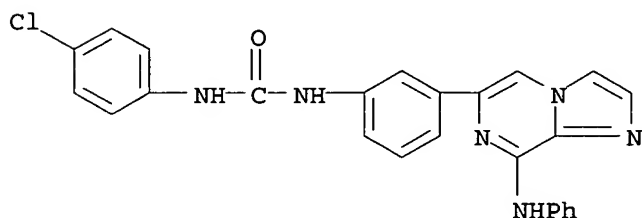
IT 618454-80-1P 618454-86-7P 618454-91-4P
618454-95-8P 618455-30-4P 618455-47-3P
618455-73-5P 618455-75-7P 618455-77-9P
618455-79-1P 618455-84-8P 618455-86-0P
618455-88-2P 618455-91-7P 618455-94-0P
618455-97-3P 618455-99-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of imidazo[1,2-a]pyrazin-8-ylamines as AKT-1 kinase inhibitors)

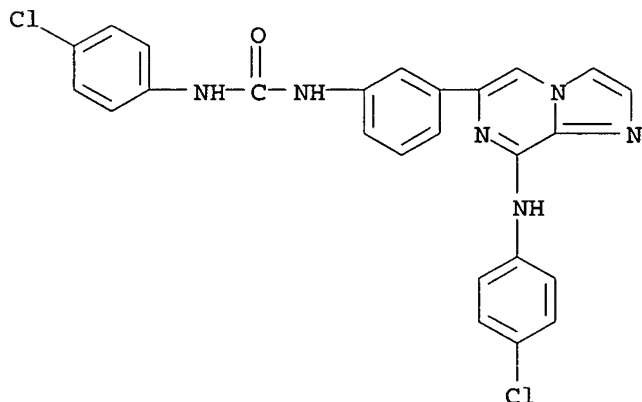
RN 618454-80-1 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



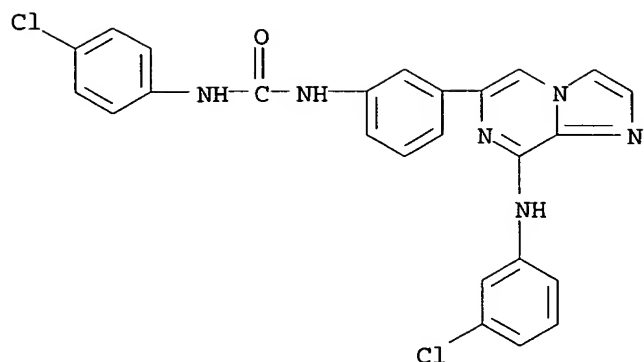
RN 618454-86-7 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



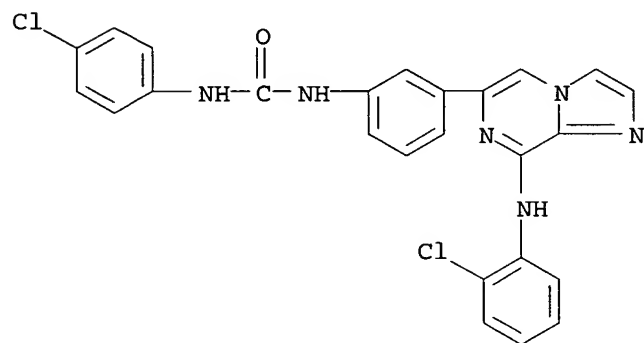
RN 618454-91-4 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



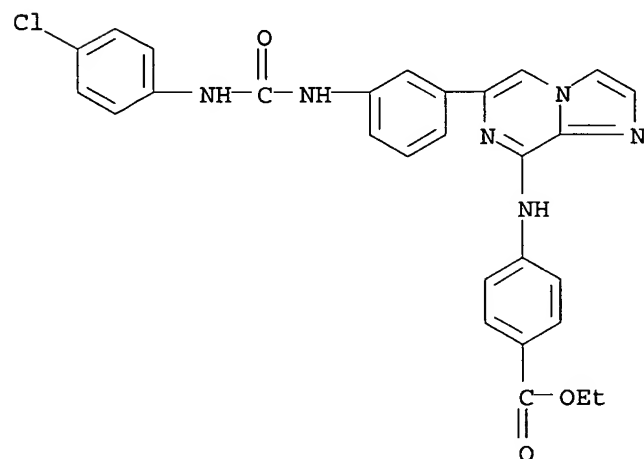
RN 618454-95-8 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



RN 618455-30-4 CAPLUS

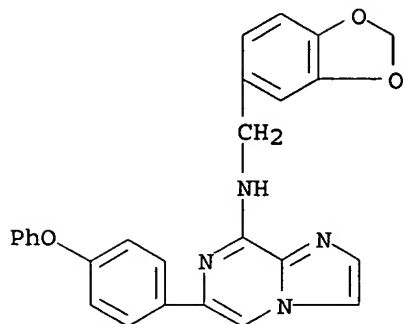
CN Benzoic acid, 4-[[6-[3-[[[(4-chlorophenyl)amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 618455-47-3 CAPLUS

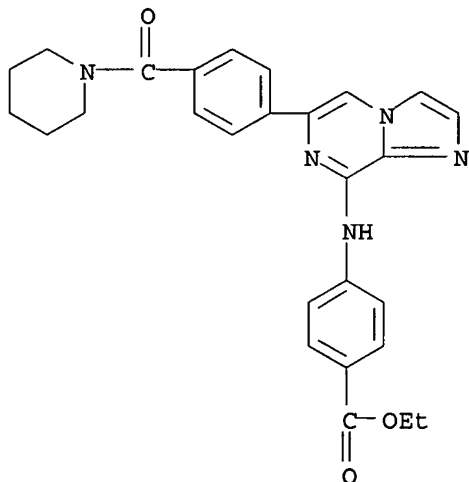
CN Imidazo[1,2-a]pyrazin-8-amine, N-(1,3-benzodioxol-5-ylmethyl)-6-(4-ethoxycarbonylphenyl)- (4-ethoxybenzoate derivative)

phenoxyphenyl) - (9CI) (CA INDEX NAME)



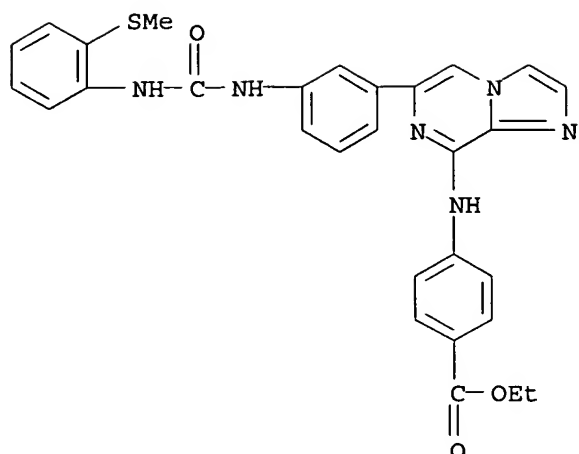
RN 618455-73-5 CAPLUS

CN Benzoic acid, 4-[[6-[4-(1-piperidinylcarbonyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



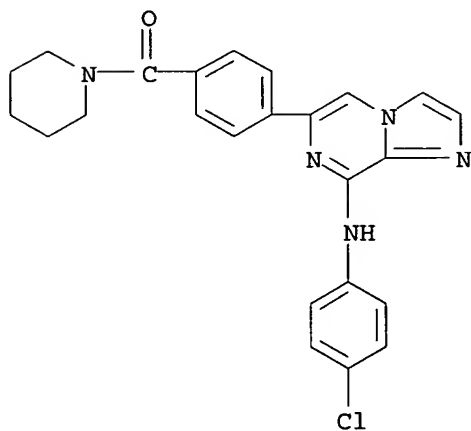
RN 618455-75-7 CAPLUS

CN Benzoic acid, 4-[[6-[3-[[[2-(methylthio)phenyl]amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



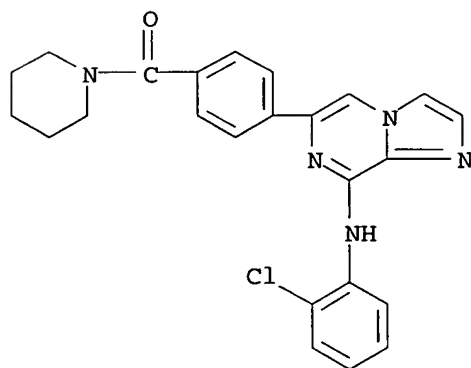
RN 618455-77-9 CAPLUS

CN Piperidine, 1-[4-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



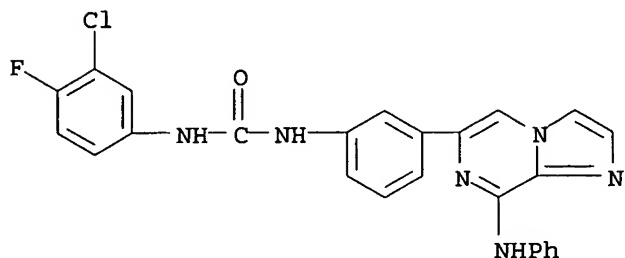
RN 618455-79-1 CAPLUS

CN Piperidine, 1-[4-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



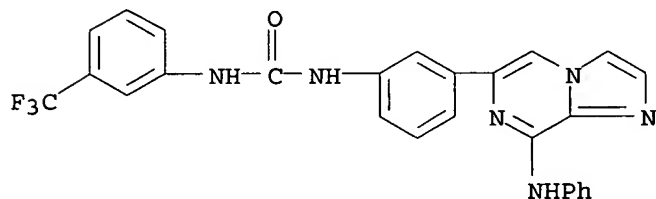
RN 618455-84-8 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



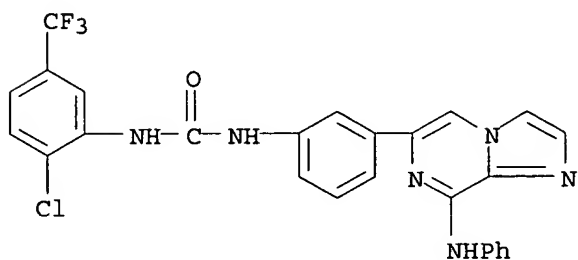
RN 618455-86-0 CAPLUS

CN Urea, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



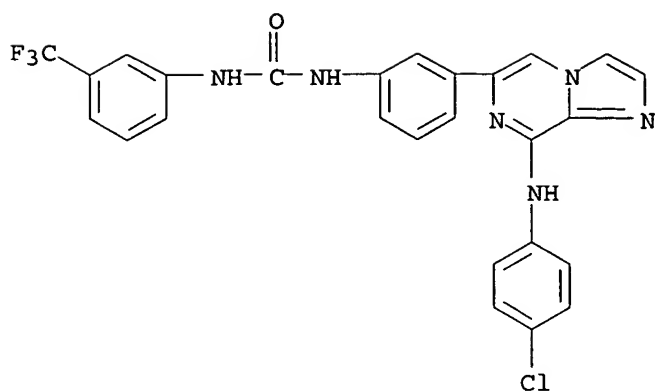
RN 618455-88-2 CAPLUS

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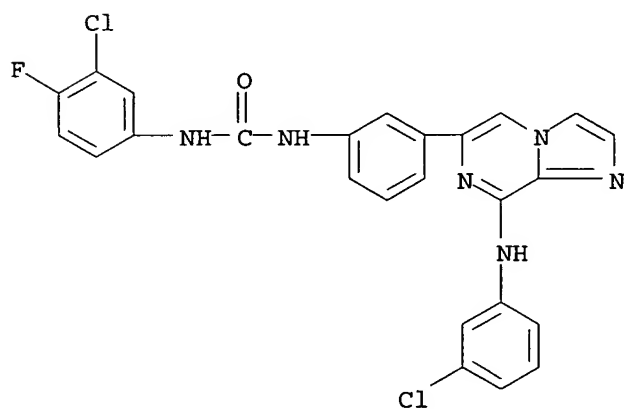
RN 618455-91-7 CAPLUS

CN Urea, N-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



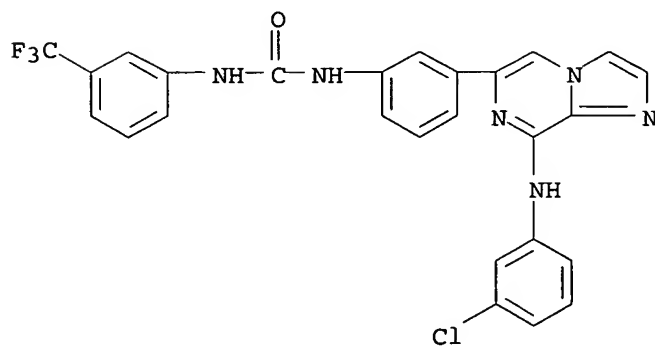
RN 618455-94-0 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 618455-97-3 CAPLUS

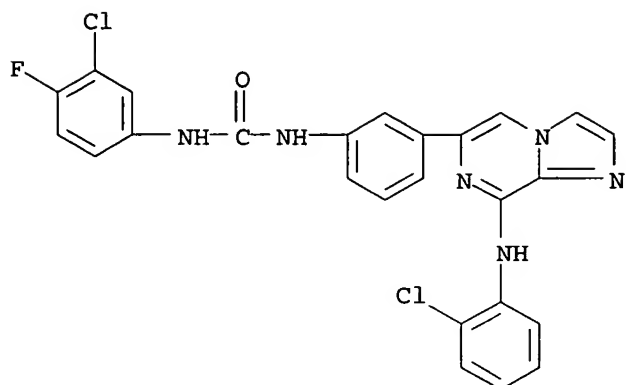
CN Urea, N-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 618455-99-5 CAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

chlorophenyl) amino] imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



L38 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:818425 CAPLUS

DOCUMENT NUMBER: 139:337987

TITLE: Preparation of imidazothienopyrazines for treatment of inflammatory and immune diseases.

INVENTOR(S): Belema, Makonen; Bunker, Amy; Nguyen, Van; Beaulieu, Francis; Ouellet, Carl; Marinier, Anne; Roy, Stephan; Yang, Xuejie; Qiu, Yuping; Zhang, Yunhui; Martel, Alain; Zusi, Christopher

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 268 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

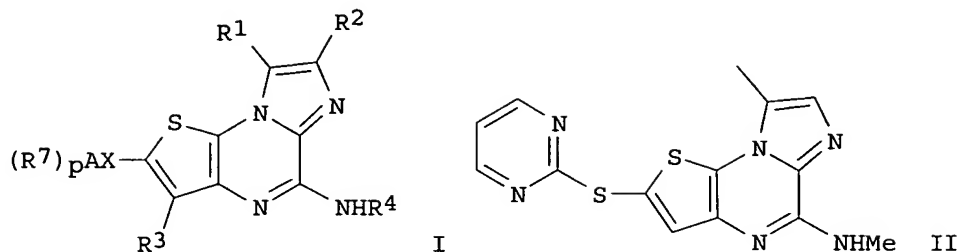
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084959	A1	20031016	WO 2003-US9549	20030327
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003222106	A1	20031020	AU 2003-222106	20030327
US 2004058930	A1	20040325	US 2003-400387	20030327
US 6933294	B2	20050823		
EP 1490371	A1	20041229	EP 2003-718092	20030327
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-369698P	P 20020403
			WO 2003-US9549	W 20030327
OTHER SOURCE(S):	MARPAT 139:337987			

ED Entered STN: 17 Oct 2003
GI



AB Title compds. [I; R1-R3 = H, halo, (perfluoro)alkyl; R4 = (CR5R6)mZ, (cycloalkyl)Z; R5, R5a, R6, R6a = H, OH, (substituted) amino, alkoxy, (cyclo)alkyl, heterocyclyl, (hetero)aryl; R7 = halo, cyano, (substituted) alkyl, alkenyl, (CR5aR6a)qOR8a, (CR5aR6a)qSR8a, (CR5aR6a)qSO2R10, (CR5aR6a)qNR8R9, (CR5aR6a)qNR8SO2, (CR5aR6a)qNR8SO2R10, (CR5aR6a)qSO2NR8R9, (CR5aR6a)qNR8aCOR9a, (CR5aR6a)qNR8aCO2R9a, (CR5aR6a)qCOR8a, (CR5aR6a)qCO2R8a, (CR5aR6a)qO2CR8a, (CR5aR6a)qCONR8aNR5R9, (CR5aR6a)qCONR8aSO2R10, cycloalkyl(alkyl), heterocyclyl(alkyl), aryl, aralkyl, heteroaryl(alkyl), etc.; when A = heterocycle, cycloalkyl, 1 of R7 may = O, when A = bond, then R7 may = H; X = bond, O, S, NR1, (CH2)n, CH:CH, C.tplbond.C; A = bond, (hetero)aryl, heterocycle, cycloalkyl; Z = H, Me, OR14, CO2R14, NR12COR13, NR12CO2R13, NR12SO2R13, NR12CONR14R15, etc.; R8, R8a, R9, R9a = H, (substituted) alkenyl, (cyclo)alkyl, (cycloalkyl)alkyl, (heterocyclyl)alkyl, aryl, aralkyl, heteroaryl, (heteroaryl)alkyl; R8R9N, R14R15N = heterocyclyl; R10, R10a = (substituted) (cyclo)alkyl, heterocyclyl, (hetero)aryl; R11 = H, (amino)alkyl, hydroxyalkyl; R12 = H, alkyl; R13 = H, (substituted) (cyclo)alkyl, heterocyclyl, (hetero)aryl; R14, R14a, R15, R15a = H, (substituted) (cyclo)alkyl, (cycloalkyl)alkyl, (heterocyclyl)alkyl, aryl(alkyl), heteroaryl(alkyl); m, q = 0-6; n = 1, 2; p = 0-4], were prepared Thus, tris(dibenzylideneacetone)dipalladium(0) and bis[(2-diphenylphosphino)phenyl]ether in toluene were bubbled with argon for 3 min; N-(2-bromo-8-methyl-1-thia-4,6,8a-triaza-as-indacen-5-yl)-N-methylamine was added followed by 2-mercaptopyrimidine and KOCMe3 in THF followed by refluxing for 2h to give 18% title compound (II).

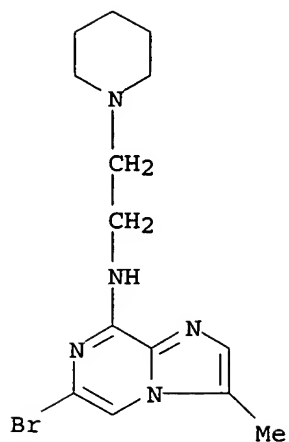
IT 615535-52-9P 615535-53-0P 615535-54-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of imidazothienopyrazines for treatment of inflammatory and immune diseases)

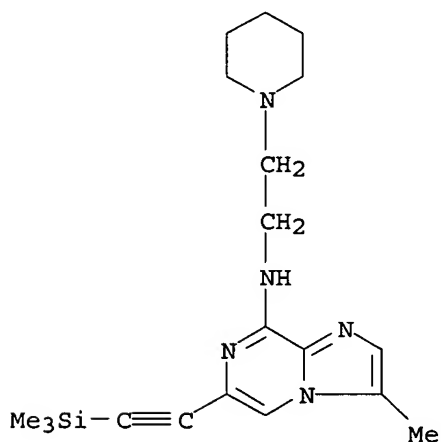
RN 615535-52-9 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-bromo-3-methyl-N-[2-(1-piperidinyl)ethyl]-(9CI) (CA INDEX NAME)



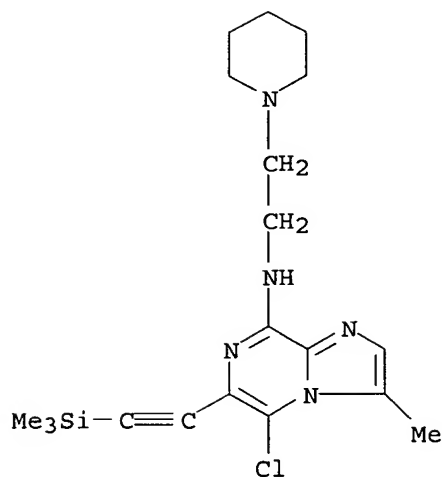
RN 615535-53-0 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-methyl-N-[2-(1-piperidinyl)ethyl]-6-[(trimethylsilyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 615535-54-1 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 5-chloro-3-methyl-N-[2-(1-piperidinyl)ethyl]-6-[(trimethylsilyl)ethynyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:594712 CAPLUS

DOCUMENT NUMBER: 137:150267

TITLE: Methods using pyrazine compounds and pyridine compounds for inhibiting JAK kinases, compound preparation, and therapeutic use

INVENTOR(S): Burns, Christopher John; Wilks, Andrew Frederick

PATENT ASSIGNEE(S): Cytopia Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060492	A1	20020808	WO 2002-AU89	20020130
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2436487	AA	20020808	CA 2002-2436487	20020130
EP 1363702	A1	20031126	EP 2002-715984	20020130
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004528295	T2	20040916	JP 2002-560683	20020130
US 2004102455	A1	20040527	US 2003-470955	20030730
US 2006069084	A1	20060330	US 2005-223633	20050909
PRIORITY APPLN. INFO.:			AU 2001-2792	A 20010130
			AU 2001-2793	A 20010130
			WO 2002-AU89	W 20020130

US 2003-470955

A3 20030730

OTHER SOURCE(S): MARPAT 137:150267

ED Entered STN: 09 Aug 2002

AB The invention provides methods of inhibiting JAK kinases involving the use of a group of compds. based either upon a 2-amino-6-carba-disubstituted pyrazine scaffold or a 2-amino-6-carba-disubstituted pyridine scaffold. The invention also provides methods of treating JAK-associated disease states.

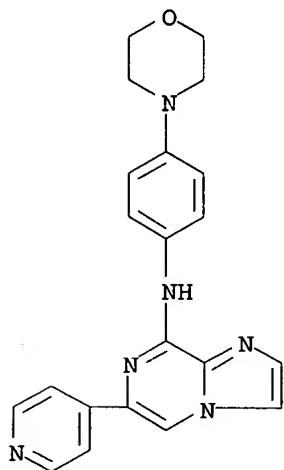
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445264-19-7 445264-21-1 445264-23-3
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445264-53-9 445264-54-0 445264-55-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pyrazine compds. and pyridine compds. for inhibiting JAK kinases, compound preparation, and therapeutic use)

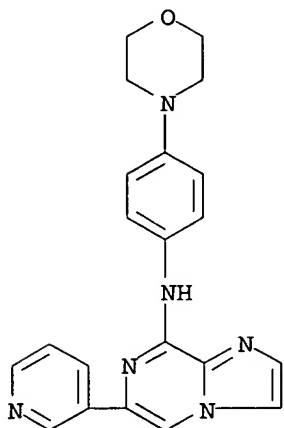
RN 445263-56-9 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(4-morpholinyl)phenyl]-6-(4-pyridinyl)-(9CI) (CA INDEX NAME)



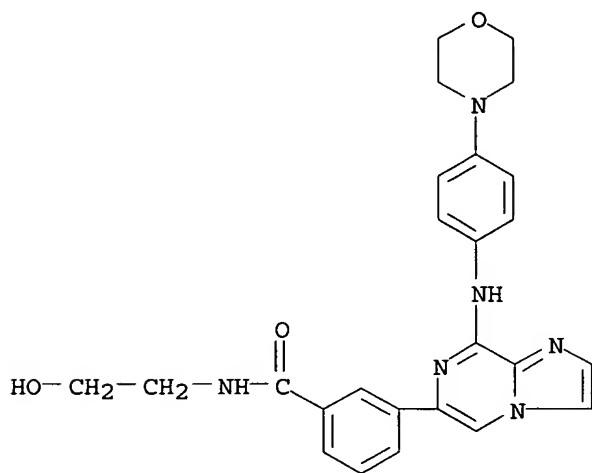
RN 445263-57-0 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(4-morpholinyl)phenyl]-6-(3-pyridinyl)-
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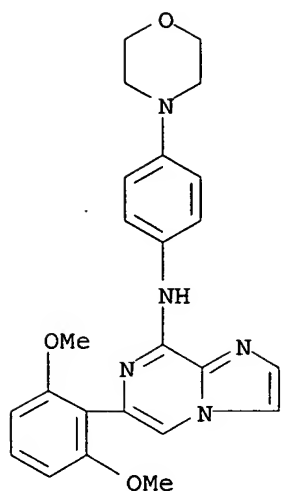
RN 445263-58-1 CAPLUS

CN Benzamide, N-(2-hydroxyethyl)-3-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo
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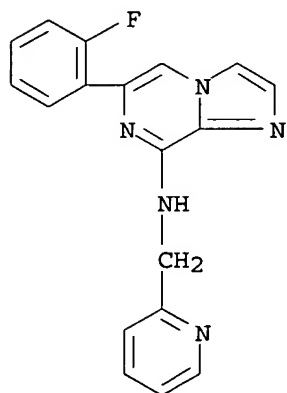
RN 445263-59-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2,6-dimethoxyphenyl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



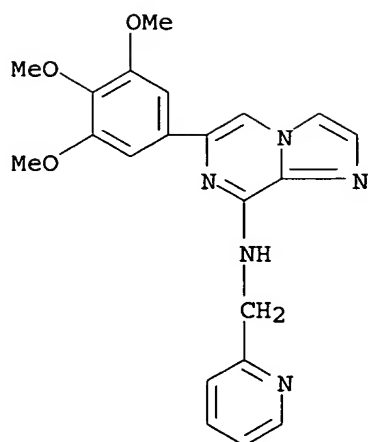
RN 445263-60-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-fluorophenyl)-N-(2-pyridinylmethyl)-
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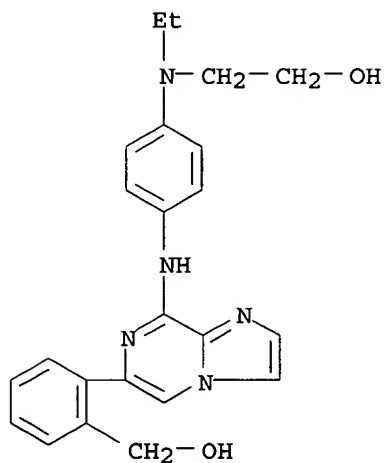
RN 445263-61-6 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-(2-pyridinylmethyl)-6-(3,4,5-
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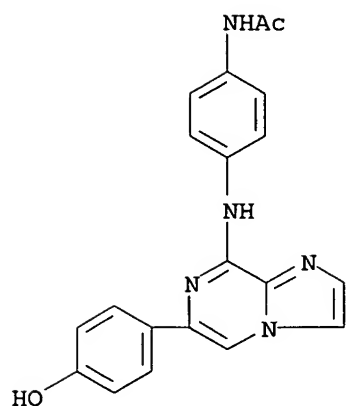
RN 445263-62-7 CAPLUS

CN Benzenemethanol, 2-[8-[[4-[ethyl(2-hydroxyethyl)amino]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



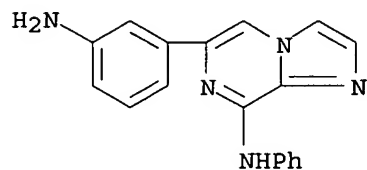
RN 445263-63-8 CAPLUS

CN Acetamide, N-[4-[[6-(4-hydroxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]- (9CI) (CA INDEX NAME)



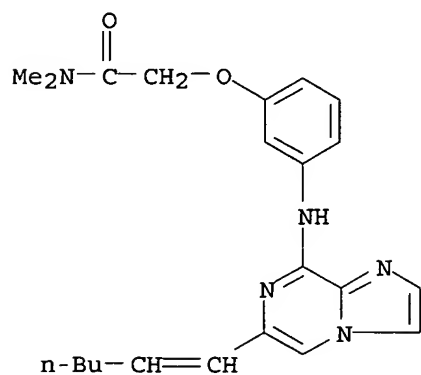
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-aminophenyl)-N-phenyl- (9CI) (CA INDEX NAME)



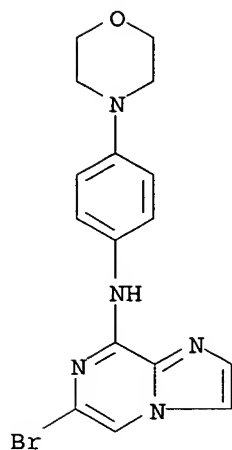
RN 445263-68-3 CAPLUS

CN Acetamide, 2-[3-[[6-(1-hexenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



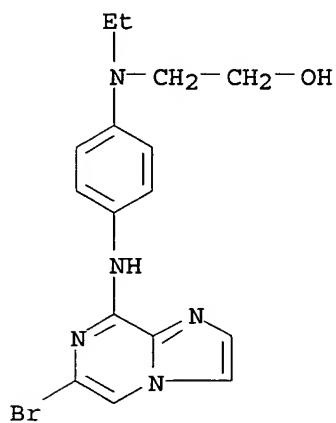
RN 445263-72-9 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-bromo-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



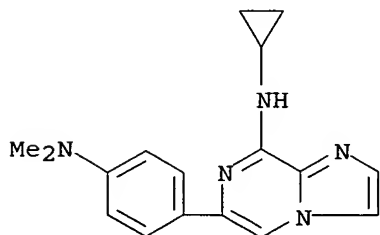
RN 445263-73-0 CAPLUS

CN Ethanol, 2-[[4-[(6-bromoimidazo[1,2-a]pyrazin-8-yl)amino]phenyl]ethylamino]- (9CI) (CA INDEX NAME)



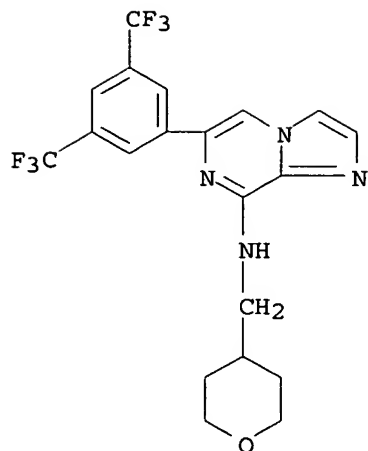
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CN Imidazo[1,2-a]pyrazin-8-amine, N-cyclopropyl-6-[4-(dimethylamino)phenyl]- (9CI) (CA INDEX NAME)



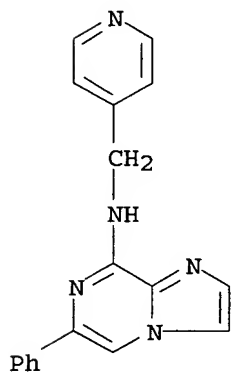
RN 445263-76-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3,5-bis(trifluoromethyl)phenyl]-N-[(tetrahydro-2H-pyran-4-yl)methyl]- (9CI) (CA INDEX NAME)



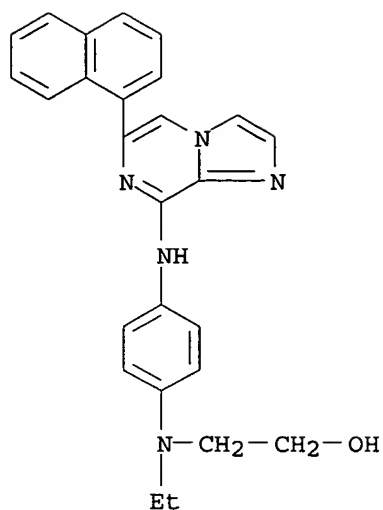
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

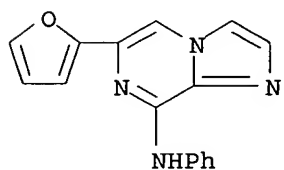


RN 445263-78-5 CAPLUS

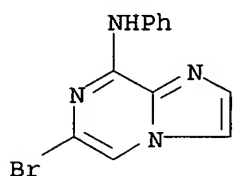
CN Ethanol, 2-[ethyl[4-[[6-(1-naphthalenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]amino]- (9CI) (CA INDEX NAME)



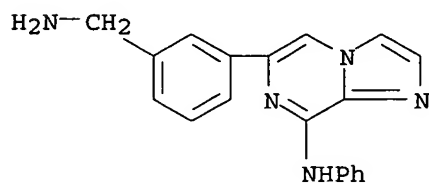
RN 445263-81-0 CAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-furanyl)-N-phenyl- (9CI) (CA INDEX NAME)



RN 445263-82-1 CAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 6-bromo-N-phenyl- (9CI) (CA INDEX NAME)

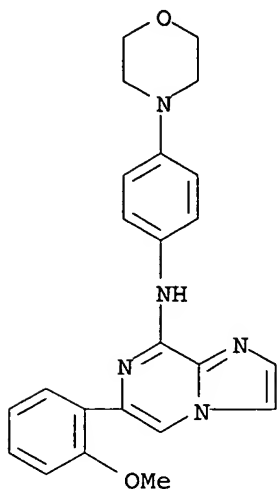


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 CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3-(aminomethyl)phenyl]-N-phenyl- (9CI) (CA INDEX NAME)



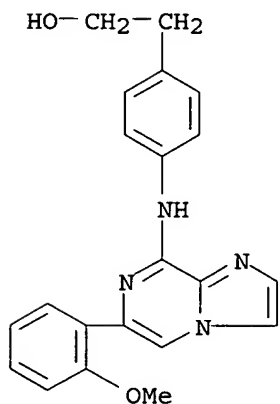
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-methoxyphenyl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



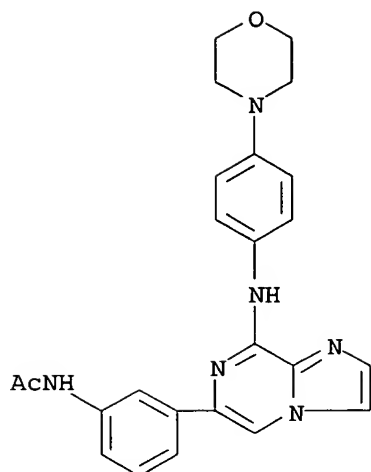
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CN Benzeneethanol, 4-[[6-(2-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



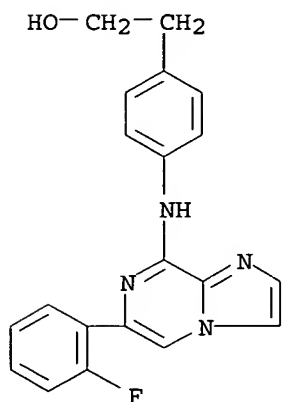
RN 445263-88-7 CAPLUS

CN Acetamide, N-[3-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



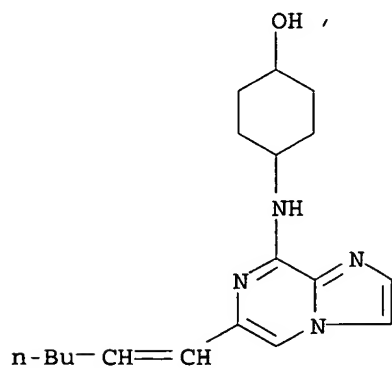
RN 445263-89-8 CAPLUS

CN Benzeneethanol, 4-[[6-(2-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino] - (9CI) (CA INDEX NAME)

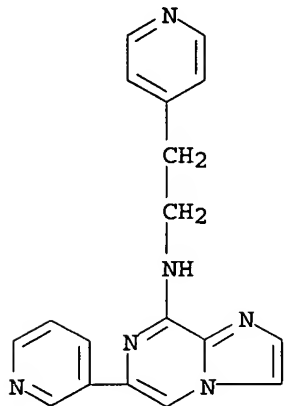


RN 445263-95-6 CAPLUS

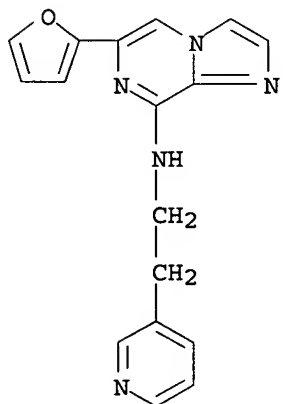
CN Cyclohexanol, 4-[[6-(1-hexenyl)imidazo[1,2-a]pyrazin-8-yl]amino] - (9CI) (CA INDEX NAME)



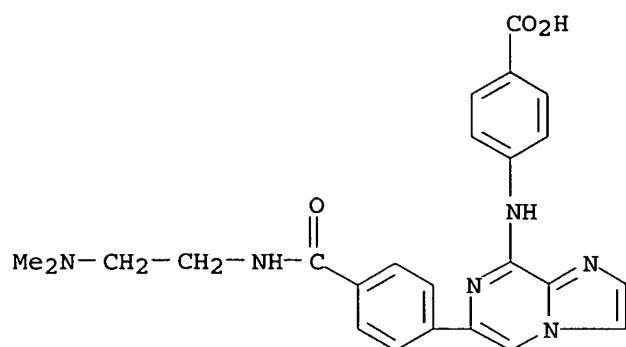
RN 445263-96-7 CAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-pyridinyl)-N-[2-(4-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)



RN 445263-97-8 CAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-furanyl)-N-[2-(3-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)

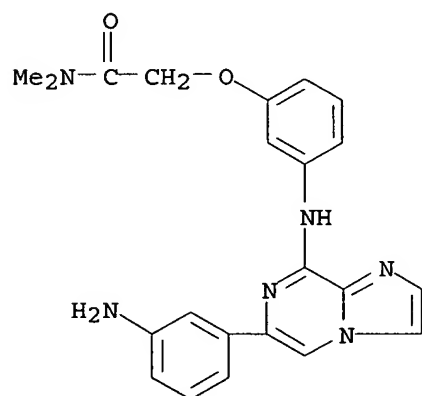


RN 445264-00-6 CAPLUS
CN Benzoic acid, 4-[[6-[4-[[[2-(dimethylamino)ethyl]amino]carbonyl]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



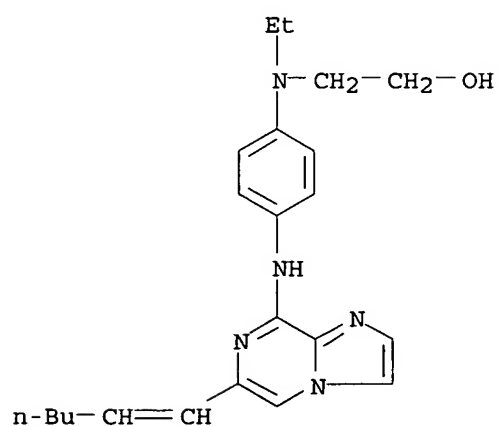
RN 445264-01-7 CAPLUS

CN Acetamide, 2-[3-[[6-(3-aminophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 445264-02-8 CAPLUS

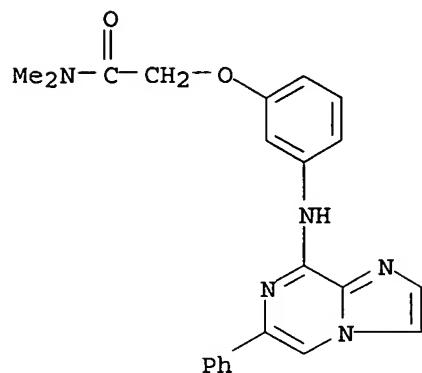
CN Ethanol, 2-[ethyl[4-[[6-(1-hexenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]amino]- (9CI) (CA INDEX NAME)



RN 445264-03-9 CAPLUS

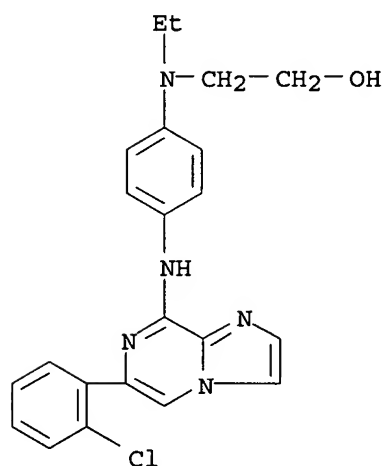
CN Acetamide, N,N-dimethyl-2-[3-[[6-phenylimidazo[1,2-a]pyrazin-8-

yl)amino]phenoxy] - (9CI) (CA INDEX NAME)



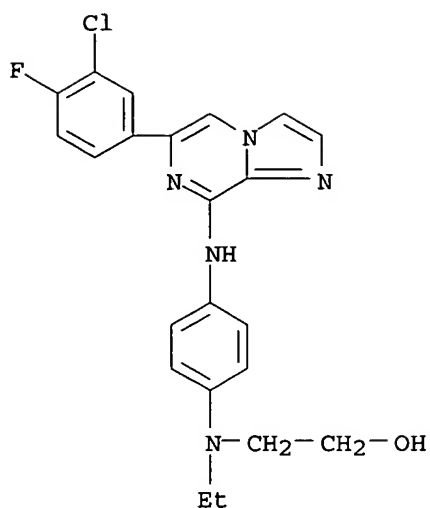
RN 445264-04-0 CAPLUS

CN Ethanol, 2-[[4-[[6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenoxy]ethylamino] - (9CI) (CA INDEX NAME)



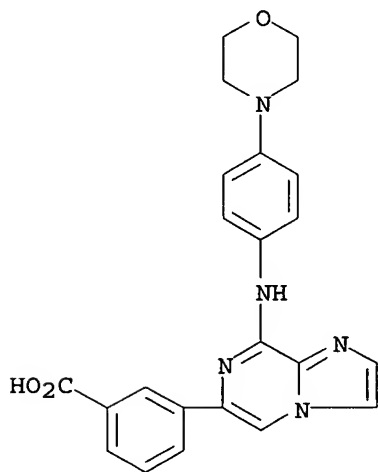
RN 445264-05-1 CAPLUS

CN Ethanol, 2-[[4-[[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenoxy]ethylamino] - (9CI) (CA INDEX NAME)



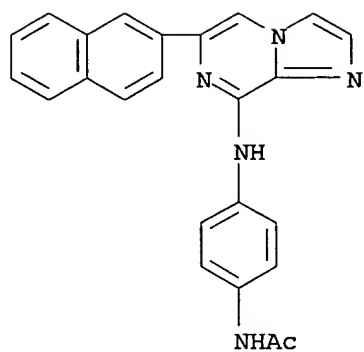
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CN Benzoic acid, 3-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



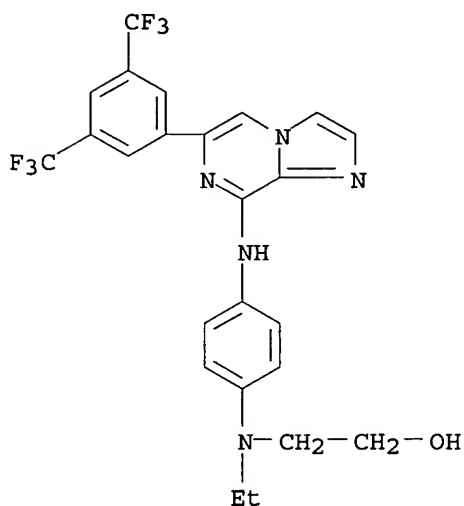
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CN Acetamide, N-[4-[[6-(2-naphthalenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]- (9CI) (CA INDEX NAME)



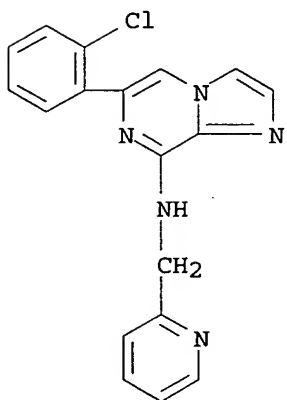
RN 445264-09-5 CAPLUS

CN Ethanol, 2-[[4-[[6-[3,5-bis(trifluoromethyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]ethylamino]- (9CI) (CA INDEX NAME)



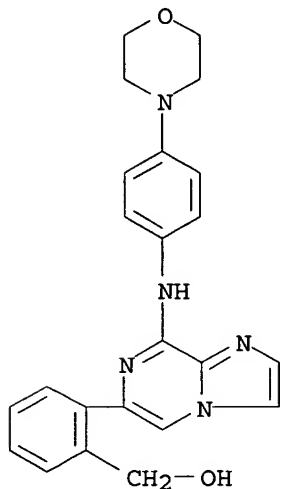
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-N-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



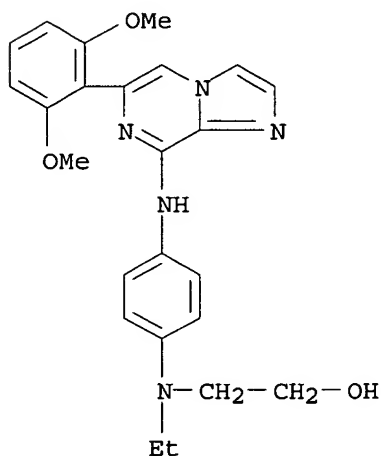
RN 445264-12-0 CAPLUS

CN Benzenemethanol, 2-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



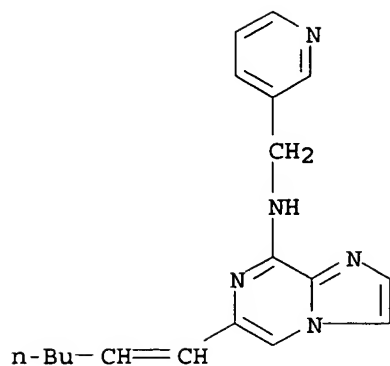
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CN Ethanol, 2-[4-[[6-(2,6-dimethoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]ethylamino]- (9CI) (CA INDEX NAME)

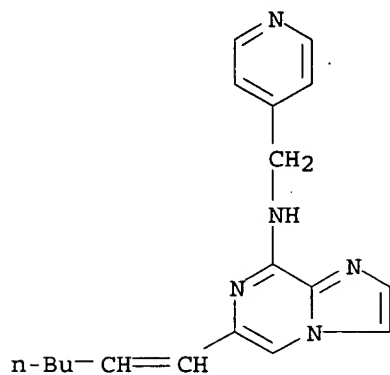


RN 445264-14-2 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1-hexenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

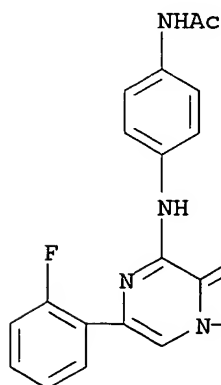


RN 445264-15-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1-hexenyl)-N-(4-pyridinylmethyl)- (9CI)
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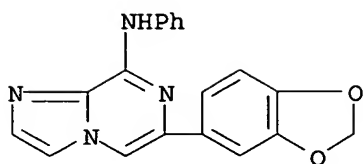
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CN Acetamide, N-[4-[[6-(2-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]- (9CI) (CA INDEX NAME)

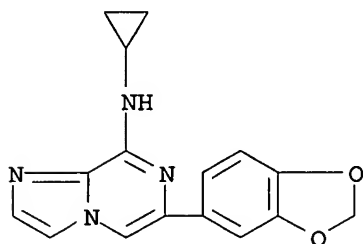


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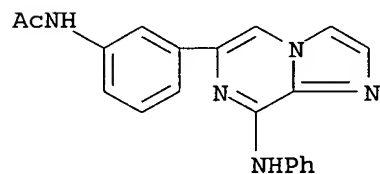
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1,3-benzodioxol-5-yl)-N-phenyl- (9CI)
(CA INDEX NAME)



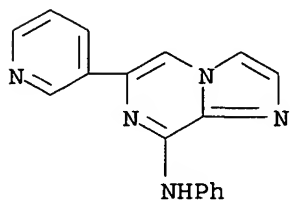
RN 445264-19-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1,3-benzodioxol-5-yl)-N-cyclopropyl-
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RN 445264-21-1 CAPLUS

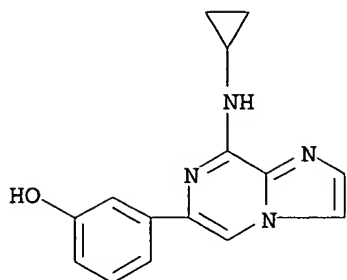
CN Acetamide, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
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CN Imidazo[1,2-a]pyrazin-8-amine, N-phenyl-6-(3-pyridinyl)- (9CI) (CA INDEX
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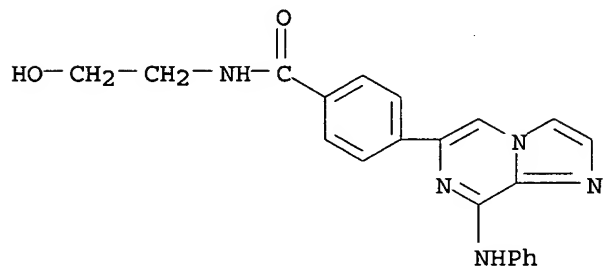
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CN Phenol, 3-[8-(cyclopropylamino)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA
INDEX NAME)



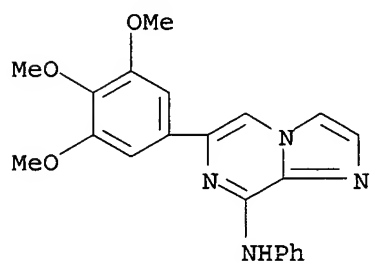
RN 445264-26-6 CAPLUS

CN Benzamide, N-(2-hydroxyethyl)-4-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl] - (9CI) (CA INDEX NAME)



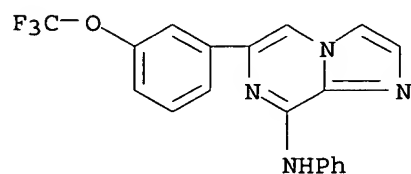
RN 445264-27-7 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-phenyl-6-(3,4,5-trimethoxyphenyl) - (9CI) (CA INDEX NAME)



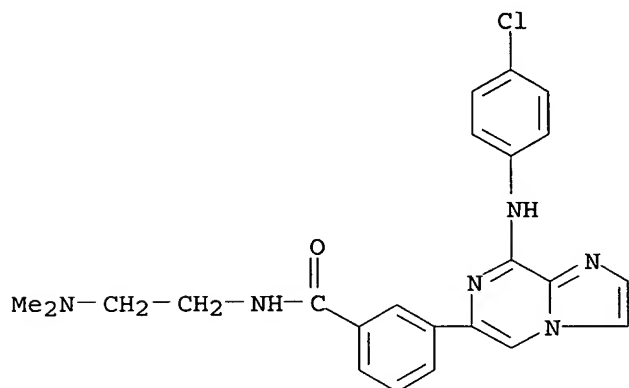
RN 445264-28-8 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-phenyl-6-[3-(trifluoromethoxy)phenyl] - (9CI) (CA INDEX NAME)



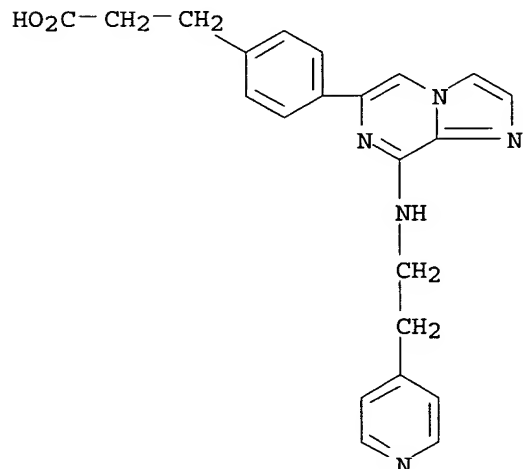
RN 445264-29-9 CAPLUS

CN Benamide, 3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



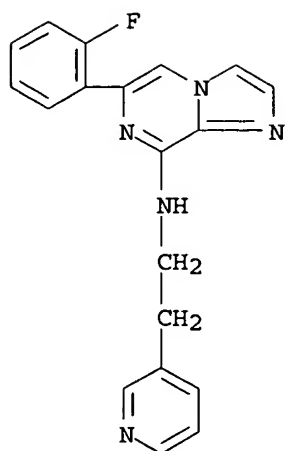
RN 445264-30-2 CAPLUS

CN Benzenepropanoic acid, 4-[8-[[2-(4-pyridinyl)ethyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



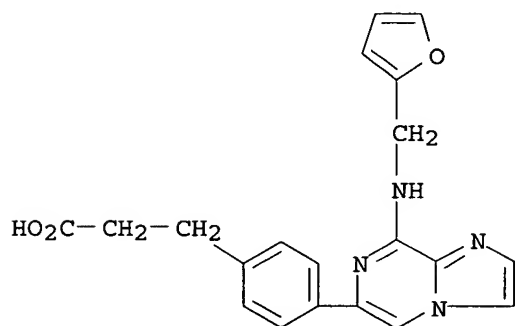
RN 445264-31-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-fluorophenyl)-N-[2-(3-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



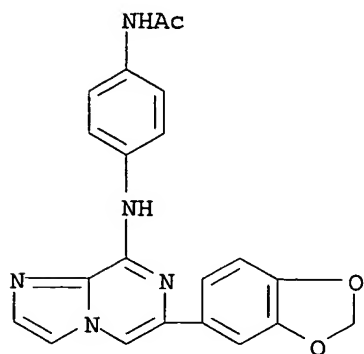
RN 445264-32-4 CAPLUS

CN Benzenepropanoic acid, 4-[8-[(2-furanylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



RN 445264-33-5 CAPLUS

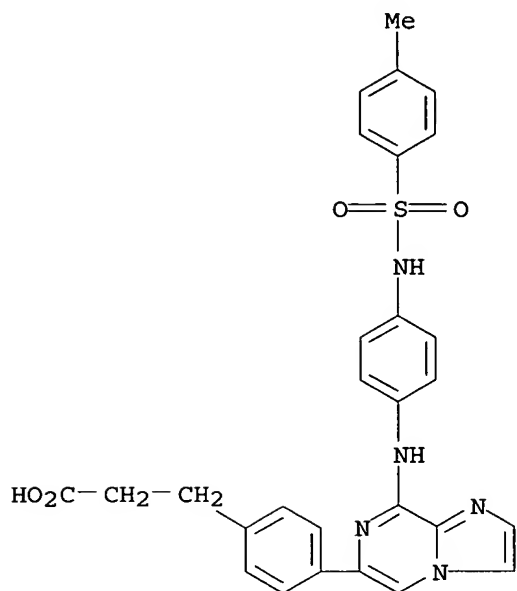
CN Acetamide, N-[4-[[6-(1,3-benzodioxol-5-yl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 445264-34-6 CAPLUS

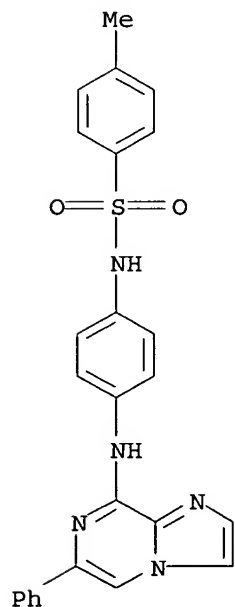
CN Benzenepropanoic acid, 4-[8-[[4-[[[4-methylphenyl)sulfonyl]amino]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]-3-phenylpropanoic acid

ino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



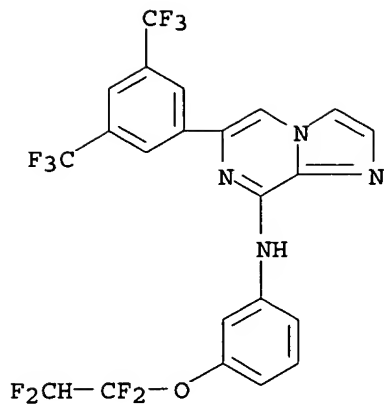
RN 445264-37-9 CAPLUS

CN Benzenesulfonamide, 4-methyl-N-[4-[(6-phenylimidazo[1,2-a]pyrazin-8-yl)amino]phenyl]- (9CI) (CA INDEX NAME)



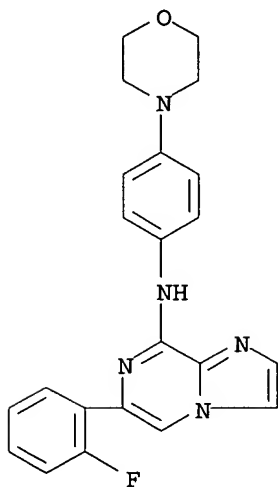
RN 445264-40-4 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3,5-bis(trifluoromethyl)phenyl]-N-[3-(1,1,2,2-tetrafluoroethoxy)phenyl]- (9CI) (CA INDEX NAME)



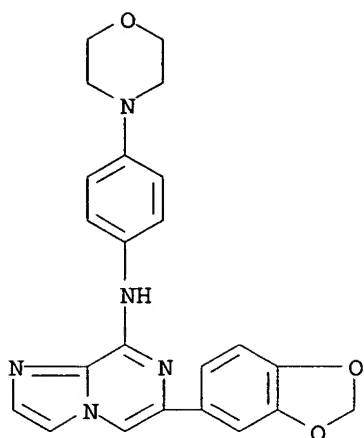
RN 445264-41-5 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-fluorophenyl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



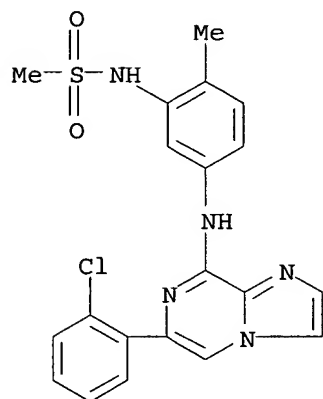
RN 445264-42-6 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1,3-benzodioxol-5-yl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



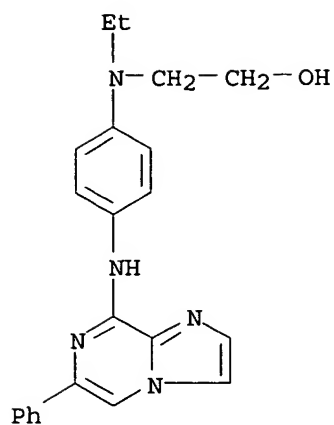
RN 445264-43-7 CAPLUS

CN Methanesulfonamide, N-[5-[[6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]- (9CI) (CA INDEX NAME)



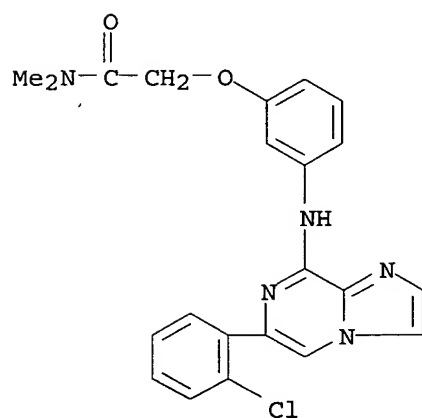
RN 445264-46-0 CAPLUS

CN Ethanol, 2-[ethyl[4-[(6-phenylimidazo[1,2-a]pyrazin-8-yl)amino]phenyl]amino]- (9CI) (CA INDEX NAME)



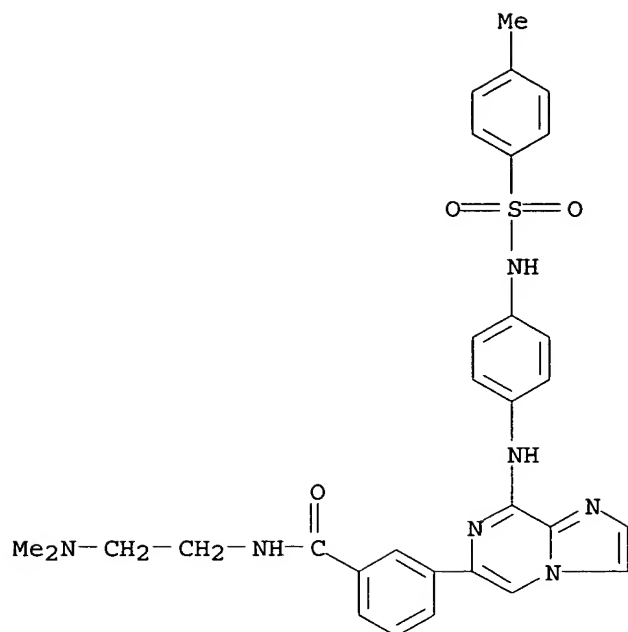
RN 445264-47-1 CAPLUS

CN Acetamide, 2-[3-[[6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



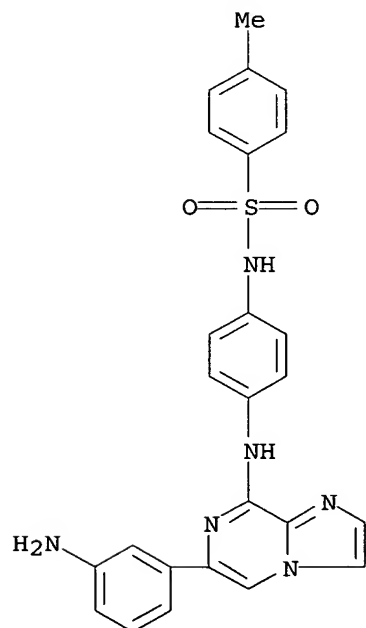
RN 445264-48-2 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-3-[8-[[4-[[4-(4-methylphenyl)sulfonyl]amino]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



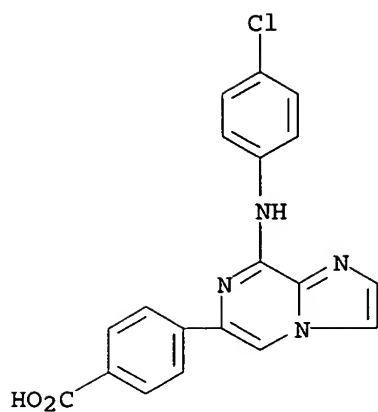
RN 445264-50-6 CAPLUS

CN Benzenesulfonamide, N-[4-[[6-(3-aminophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]-4-methyl- (9CI) (CA INDEX NAME)



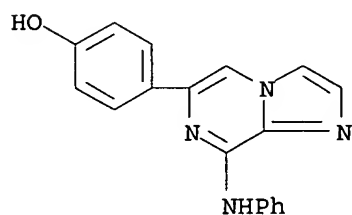
RN 445264-51-7 CAPLUS

CN Benzoic acid, 4-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



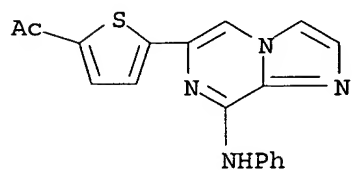
RN 445264-52-8 CAPLUS

CN Phenol, 4-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



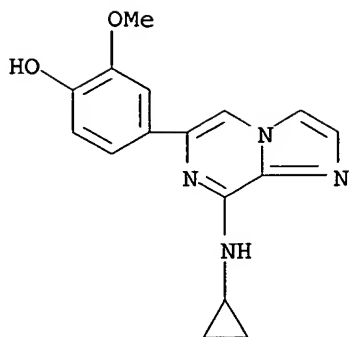
RN 445264-53-9 CAPLUS

CN Ethanone, 1-[5-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]-2-thienyl]- (9CI) (CA INDEX NAME)

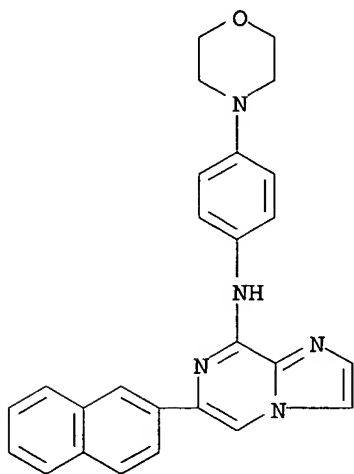


RN 445264-54-0 CAPLUS

CN Phenol, 4-[8-(cyclopropylamino)imidazo[1,2-a]pyrazin-6-yl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 445264-55-1 CAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(4-morpholinyl)phenyl]-6-(2-naphthalenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:757953 CAPLUS
 DOCUMENT NUMBER: 130:133638
 TITLE: Antiproliferative, differentiating and apoptotic effects elicited by imidazo[1,2-a]pyrazine derivatives
 AUTHOR(S): Zurbonsen, K.; Michel, A.; Bonnet, P. A.; Mathieu, M. N.; Chevillard, C.
 CORPORATE SOURCE: INSERM U.469 ORGANIQUE PHARMACEUTIQUE FACULTE DE PHARMACIE, MONTPELLIER, 34094, Fr.
 SOURCE: General Pharmacology (1998), Volume Date 1999, 32(1), 135-141
 CODEN: GEPHDP; ISSN: 0306-3623
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 03 Dec 1998
 AB The activity of two series of imidazo[1,2-a]pyrazine derivs. on cell proliferation and differentiation and on apoptosis was examined in relation

to their effects on phosphodiesterase (PDE) activity and on purinoceptors. In the first series SC-8 and SC-51 inhibited mitogen-induced 3H-thymidine incorporation in human lymphocytes. The compds. of the new series PAB13, PAB23 and SCA40 inhibited the proliferation of the HEL cell line. 4. Nine imidazo[1,2-a]pyrazine derivs. of the new series have been studied on the Dami cell proliferation. SCA41 and SCA44 inhibited cell growth, SCA40 and PAB40 were moderately effective, whereas PAB12 and PAB30 were devoid of effect. The antiproliferative effects of these six non-cytotoxic compds. could not be related to their action on PDE or on purinoceptors, but rather to their lipophilicity. Conversely, for PAB13, PAB15, and PAB23, the decrease in cell number was related to their cytotoxic and apoptotic effects through their cAMP-increasing and PDE-inhibitory potency, but unrelated to an effect on purinoceptors. Imidazo[1,2-a]pyrazine derivs. decreased the expression of Glycoprotein (GP)Ib in Dami cells while some of them enhanced that of GPIIb/IIIa. These effects appeared to involve inhibition of both cAMP- and cGMP-PDE. These studies demonstrate the potential interest of imidazo[1,2-a]pyrazine derivs. in the query of novel anticancer drugs.

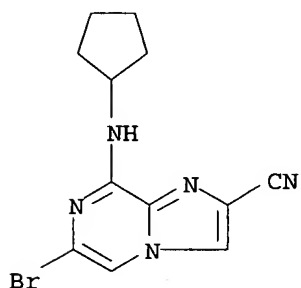
IT 193343-21-4, SCA44

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiproliferative, differentiating and apoptotic effects of imidazo[1,2-a]pyrazine derivs.)

RN 193343-21-4 CAPLUS

CN Imidazo[1,2-a]pyrazine-2-carbonitrile, 6-bromo-8-(cyclopentylamino)- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:573167 CAPLUS

DOCUMENT NUMBER: 127:257111

TITLE: Antiproliferative effects of imidazo[1,2-a]pyrazine derivatives on the dami cell line

AUTHOR(S): Zurbonsen, Katja; Michel, Alain; Vittet, Daniel; Bonnet, Pierre-Antoine; Chevillard, Claude

CORPORATE SOURCE: INSERM U.300, FACULTE DE PHARMACIE, MONTPELLIER, 34060, Fr.

SOURCE: Biochemical Pharmacology (1997), 54(3), 365-371
CODEN: BCPA6; ISSN: 0006-2952

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Sep 1997

AB Since cyclic 3',5'-adenosine monophosphate (cAMP) is involved in cell

proliferation and as previous data showed that imidazo[1,2- α]pyrazine derivs. (PAB12, PAB30, PAB40, SCA40, SCA41, and SCA44) inhibited cAMP breakdown by a phosphodiesterase (PDE)-inhibitory effect, the aim of the present study was to investigate the effects of these derivs. on proliferation of the Dami cell line in relation with their actions on cAMP content and on PDE isoenzymes isolated from Dami cells. SCA41 and SCA44 inhibited cell growth in a dose-dependent manner, while SCA40 and PAB40 induced a weak inhibition. Growth inhibitions were 40%, 91%, and 60% for SCA41, SCA44 (at 100 μ M), and IBMX (at 1000 μ M), resp., and could not be related to their effects on cAMP levels. In addition, although all compds. potentiated cAMP formation by prostaglandin E1 (PGE1), no potentiations were observed when the antiproliferative effects of SCA41 and SCA44 were considered. Investigation of derivs. on PDE isoenzymes III, IV, and V indicated non-selective PDE inhibitory effects for SCA41 and SCA44, while SCA40 elicited preferences for type III, and PAB30 and PAB40 preferences for type IV isoenzymes. These effects could not totally explain the antiproliferative activity of the derivs. The activation of P2 purinoceptors by imidazo[1,2- α]pyrazine did not lead to their antiproliferative effects. Thus, the mechanism of the antiproliferative effects of the compds. remains to be determined. It does, however, depend on the chemical substitutions of the imidazo[1,2- α]pyrazine skeleton and in particular on the 2-carbonitrile presence and the length of the 8-aminoaliph. group.

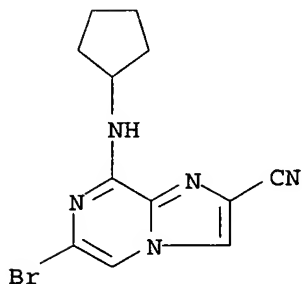
IT 193343-21-4, SCA44

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiproliferative structure activity relations of imidazo[1,2- α]pyrazine derivs. on the dami cell line)

RN 193343-21-4 CAPLUS

CN Imidazo[1,2- α]pyrazine-2-carbonitrile, 6-bromo-8-(cyclopentylamino)- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:424066 CAPLUS

DOCUMENT NUMBER: 127:145144

TITLE: Modulation of the megakaryoblastic Dami cell line differentiation by phosphodiesterase inhibitors and imidazo[1,2- α]pyrazine derivatives

AUTHOR(S): Zurbonsen, Katja; Michel, Alain; Vittet, Daniel; Bonnet, Pierre-Antoine; Chevillard, Claude

CORPORATE SOURCE: INSERM U.300, Faculty de Pharmacy, Montpellier, F-34060, Fr.

SOURCE: Pharmacology & Toxicology (Copenhagen) (1997), 80(6),

286-289

CODEN: PHTOEH; ISSN: 0901-9928

PUBLISHER:

Munksgaard

DOCUMENT TYPE:

Journal

LANGUAGE:

English

ED Entered STN: 09 Jul 1997

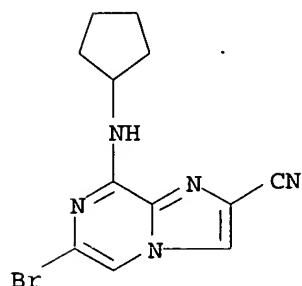
AB Phosphodiesterase inhibitors have been shown to modulate cell differentiation. The authors have previously shown that a series of imidazo[1,2-a]pyrazine derivs. displayed inhibitory effects on phosphodiesterase isoenzymes types III, IV and V isolated from Dami cells and on Dami cell growth. In the present study the authors have investigated the effect of these derivs. on the expression of two differentiation markers, glycoproteins Ib and IIb/IIIa of the human megakaryoblastic leukemic Dami cell line in comparison to those elicited by 3-isobutyl-1-methylxanthine and selective phosphodiesterase inhibitors of type I (8-methoxymethyl-1-methyl-3-(2-methylpropyl)xanthine), III (Milrinone), IV (RO-201724) and V (Zaprinast). Imidazo[1,2-a]pyrazine derivs., 3-isobutyl-1-methylxanthine and selective phosphodiesterase inhibitors, except 8-methoxymethyl-1-methyl-3-(2-methylpropyl) xanthine, decreased glycoprotein Ib expression. SCA40, SCA41, SCA44 and 3-isobutyl-1-methylxanthine but not the other compds. affected the expression of glycoprotein IIb/IIIa in a pos. manner. The effects of imidazo[1,2-a]pyrazine derivs. on glycoprotein expression appeared to be related to their phosphodiesterase inhibitory potency.

IT 193343-21-4, SCA 44

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(modulation of megakaryoblastic Dami cell line differentiation by phosphodiesterase inhibitors and imidazo[a]pyrazine derivs. determined by glycoprotein expression)

RN 193343-21-4 CAPLUS

CN Imidazo[1,2-a]pyrazine-2-carbonitrile, 6-bromo-8-(cyclopentylamino)- (9CI)
(CA INDEX NAME)

L38 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:631072 CAPLUS

DOCUMENT NUMBER: 109:231072

TITLE: 8-Alkylaminoimidazo[1,2-a]pyrazine derivatives, their preparation, and their application in therapy

INVENTOR(S): Sablayrolles, Claire; Bonnet, Pierre Antoine; Cros, Gerard; Chapat, Jean Pierre; Boucard, Maurice

PATENT ASSIGNEE(S): Byk-Gulden Lomberg Chemische Fabrik G.m.b.H., Fed. Rep. Ger.

SOURCE: PCT Int. Appl., 41 pp.

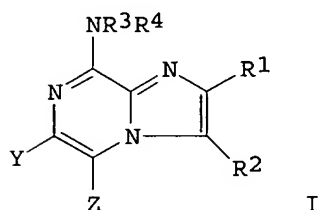
CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8804298	A1	19880616	WO 1987-EP756	19871204
W: JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
FR 2607813	A1	19880610	FR 1986-17164	19861205
FR 2607813	B1	19890331		
EP 348392	A1	19900103	EP 1988-900690	19871204
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02501575	T2	19900531	JP 1988-500907	19871204
US 5028605	A	19910702	US 1989-364428	19890602
PRIORITY APPLN. INFO.:			FR 1986-17164	A 19861205
			WO 1987-EP756	W 19871204
OTHER SOURCE(S): CASREACT 109:231072; MARPAT 109:231072				
ED Entered STN: 24 Dec 1988				
GI				

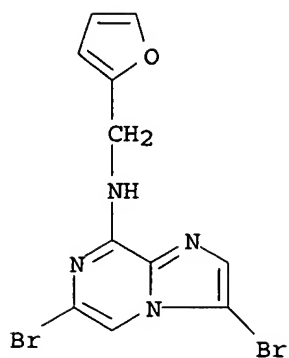


AB The title compds. [I; R1,R2 = H, CF3, NO, NO2, cyano, halo, C1-5 alkyl, alkoxy, carbonyl, (substituted) Ph, carbamoyl, cycloalkyl, acyl, alkylthio; R1R2 = (CH2)4; R3, R4 = H; (substituted) C1-5 alkyl, acyl, furfuryl; R3R4 = (CH2)5, CH2CH2OCH2CH2, CH2CH2SCH2CH2; Y, Z = H, halo, CO2H, cyano, C1-5 alkyl, alkoxy, CF3, amino] and their pharmaceutically compatible salts were prepared as antispasmodics, uterine relaxants, bronchodilators, cardiac analeptics, and neurosedatives. Imidazo[1,2-a]pyrazine (preparation, from aminopyrazine, given), in HOAc was treated with Br in HOAc and the product 3,5-dibromoimidazo[1,2-a]pyrazine was stirred with aqueous MeNH2 to give 3-bromo-8-methylaminoimidazo[1,2-a]pyrazine. I had ED50's 13-40 times greater than theophylline (II) for antispasmodic activity in rat duodenum.

IT 117718-79-3P 117736-93-3P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as drug)

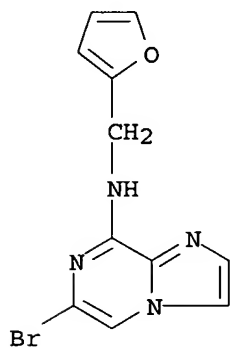
RN 117718-79-3 CAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3,6-dibromo-N-(2-furanylmethyl)- (9CI) (CA INDEX NAME)



RN 117736-93-3 CAPLUS

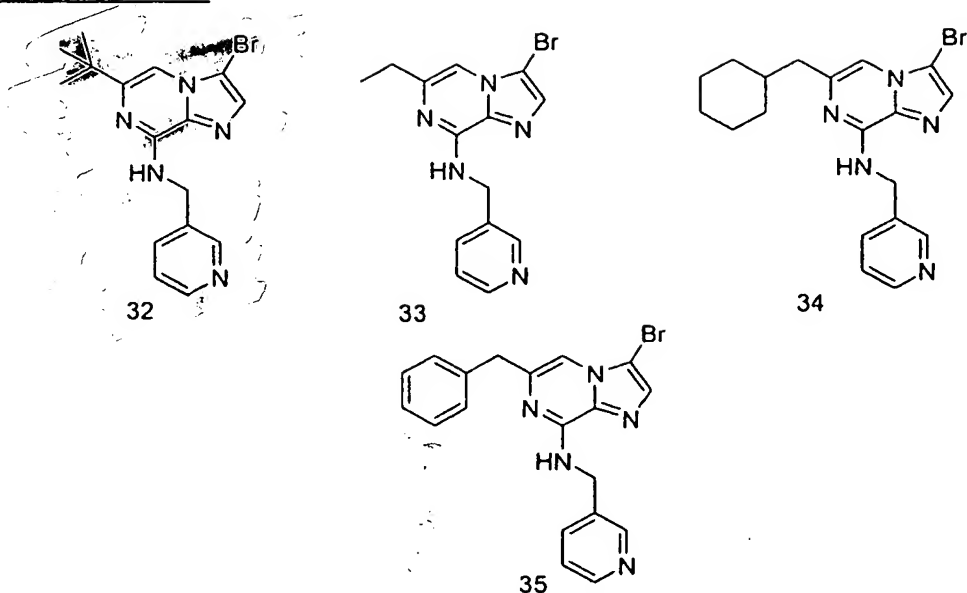
CN Imidazo[1,2-a]pyrazin-8-amine, 6-bromo-N-(2-furanylmethyl)- (9CI) (CA
INDEX NAME)



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EXAMPLES 32-35:

These compounds are prepared by essentially same procedure set forth in Preparative Example 31.

- 5 **ASSAY:** The assay on the compounds of the invention can be performed as described below:

BACULOVIRUS CONSTRUCTIONS: Cyclins A and E are cloned into pVL1393 (Pharmingen, La Jolla, California) by PCR, with the addition of 5 histidine residues at the amino-terminal end to allow purification on nickel resin.

- 10 The expressed protein is approximately 46kDa (cyclin E) and 50kDa (cyclin A) in size. CDK2 was cloned into pVL1393 by PCR, with the addition of a haemagglutinin epitope tag at the carboxy-terminal end (YDVPDYAS). The expressed protein is approximately 34kDa in size.

- ENZYME PRODUCTION:** Recombinant baculoviruses expressing cyclins
- 15 A, E and CDK2 are co-infected into SF9 cells at an equal multiplicity of infection (MOI=5), for 48 hrs. Cells are harvested by centrifugation at 1000 RPM for 10 minutes, then pellets lysed on ice for 30 minutes in five times the pellet volume of lysis buffer containing 50mM Tris pH 8.0, 150mM NaCl, 1% NP40, 1mM DTT and protease inhibitors (Roche Diagnostics GmbH, Mannheim, Germany).
- 20 Lysates are spun down at 15000 RPM for 10 minutes and the supernatant retained. 5ml of nickel beads (for one liter of SF9 cells) are washed three times in

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